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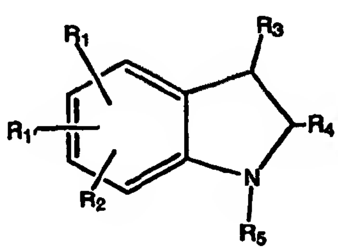
(54) Title: INHIBITORS OF PHOSPHOLIPASE ENZYMES



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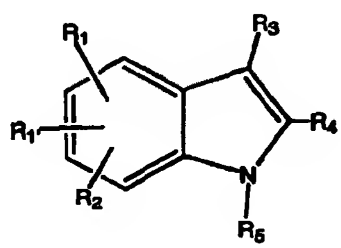

(II)

(57) Abstract

This invention concerns compounds and pharmaceutical compositions useful for treating or preventing inflammatory conditions in a mammal, the methods comprising administration of novel pharmaceutically useful compounds of general formulae (I) or (II) or pharmaceutically acceptable salts thereof, wherein R_1–R_5 are as defined in the specification.

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INHIBITORS OF PHOSPHOLIPASE ENZYMES

Background of the Invention

The present invention relates to chemical inhibitors of the activity of various phospholipase enzymes, particularly phospholipase A_2 enzymes.

Leukotrienes and prostaglandins are important mediators of inflammation, each of which classes contributes to the development of an inflammatory response in a different way. Leukotrienes recruit inflammatory cells such as neutrophils to an inflamed site, promote the extravasation of these cells and stimulate release of superoxide and proteases which damage the tissue. Leukotrienes also play a pathophysiological role in the hypersensitivity experienced by asthmatics [See, e.g. B. Samuelson et al., Science, 237:1171-76 (1987)]. Prostaglandins enhance inflammation by increasing blood flow and therefore infiltration of leukocytes to inflamed sites. Prostaglandins also potentiate the pain response induced by stimuli.

Prostaglandins and leukotrienes are unstable and are not stored in cells, but are instead synthesized [W. L. Smith, Biochem. J., 259:315-324 (1989)] from arachidonic acid in response to stimuli. Prostaglandins are produced from arachidonic acid by the action of COX-1 and COX- 2 enzymes. Arachidonic acid is also the substrate for the distinct enzyme pathway leading to the production of leukotrienes.

Arachidonic acid which is fed into these two distinct inflammatory pathways is released from the sn-2 position of membrane phospholipids by phospholipase A_2 enzymes (hereinafter PLA_2). The reaction catalyzed by PLA_2 is believed to represent the rate-limiting step in the process of lipid mediated biosynthesis and the production of inflammatory prostaglandins and leukotrienes. When the phospholipid substrate of PLA_2 is of the phosphotidyl choline class with an ether linkage in the sn-1 position, the lysophospholipid produced is the immediate precursor of platelet activating factor (hereafter called PAF), another potent mediator of inflammation [S.I. Wasserman, Hospital Practice, 15:49-58 (1988)].

Most anti-inflammatory therapies have focussed on preventing production of either prostglandins or leukotrienes from these distinct pathways, but not on all of them. For

example, ibuprofen, aspirin, and indomethacin are all NSAIDs which inhibit the production of prostaglandins by COX-1/COX-2, but have no effect on the inflammatory production of leukotrienes from arachidonic acid in the other pathways. Conversely, zileuton inhibits only the pathway of conversion of arachidonic acid to leukotriense, without affecting the production of prostaglandins. None of these widely-used anti-inflammatory agents affects the production of PAF.

Consequently the direct inhibition of the activity of PLA_2 has been suggested as a useful mechanism for a therapeutic agent, i.e., to interfere with the inflammatory response. [See, e.g., J. Chang et al, Biochem. Pharmacol., 36:2429-2436 (1987)].

A family of PLA_2 enzymes characterized by the presence of a secretion signal sequenced and ultimately secreted from the cell have been sequenced and structurally defined. These secreted PLA_2s have an approximately 14 kD molecular weight and contain seven disulfide bonds which are necessary for activity. These PLA_2s are found in large quantities in mammalian pancreas, bee venom, and various snake venom. [See, e.g., references 13-15 in Chang et al, cited above; and E. A. Dennis, Drug Devel. Res., 10:205-220 (1987).] However, the pancreatic enzyme is believed to serve a digestive function and, as such, should not be important in the production of the inflammatory mediators whose production must be tightly regulated.

The primary structure of the first human non-pancreatic PLA_2 has been determined. This non-pancreatic PLA_2 is found in platelets, synovial fluid, and spleen and is also a secreted enzyme. This enzyme is a member of the aforementioned family. [See, J. J. Seilhamer et al, J. Biol. Chem., 264:5335-5338 (1989); R. M. Kramer et al, J. Biol. Chem., 264:5768-5775 (1989); and A. Kando et al, Biochem. Biophys. Res. Comm., 163:42-48 (1989)]. However, it is doubtful that this enzyme is important in the synthesis of prostaglandins, leukotrienes and PAF, since the non-pancreatic PLA_2 is an extracellular protein which would be difficult to regulate, and the next enzymes in the biosynthetic pathways for these compounds are intracellular proteins. Moreover, there is evidence that PLA_2 is regulated by protein kinase C and G proteins [R. Burch and J. Axelrod, Proc. Natl. Acad. Sci. U.S.A., 84:6374-6378 (1989)] which are cytosolic proteins which must act on intracellular proteins. It would be impossible for the non-pancreatic PLA_2 to function in the cytosol, since the high reduction potential would reduce the disulfide bonds and inactivate the enzyme.

A murine PLA_2 has been identified in the murine macrophage cell line, designated RAW 264.7. A specific activity of 2 mols/min/mg, resistant to reducing conditions, was

reported to be associated with the approximately 60 kD molecule. However, this protein was not purified to homogeneity. [See, C. C. Leslie et al, Biochem. Biophys. Acta., 963:476-492 (1988)]. The references cited above are incorporated by reference herein for information pertaining to the function of the phospholipase enzymes, particularly PLA_2.

A cytosolic phospholipase A_2 (hereinafter "$cPLA_2$") has also been identified and cloned. See, U.S. Patent Nos. 5,322,776 and 5,354,677, which are incorporated herein by reference as if fully set forth. The enzyme of these patents is an intracellular PLA_2 enzyme, purified from its natural source or otherwise produced in purified form, which functions intracellularly to produce arachidonic acid in response to inflammatory stimuli.

It is now desirable to identify pharmaceutically useful compounds which inhibit the actions of these phospholipase enzymes for use in treating or preventing inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes and PAF are all desired results. There remains a need in the art for an identification of such anti-inflammatory agents for therapeutic use in a variety of disease states.

Numerous pieces of evidence have supported the central role of $cPLA_2$ in lipid mediator biosynthesis: $cPLA_2$ is the only enzyme which is highly selective for phospholipids containing arachidonic acid in the *sn*-2 position (Clark et al., 1991, 1995; Hanel & Gelb, 1993); activation of $cPLA_2$ or its increased expression have been linked with increased leukotriene and prostaglandin synthesis (Lin et al., 1992a, 1992b, 1993); and following activation, $cPLA_2$ translocates to the nuclear membrane, where it is co-localized with the cyclooxygenase and lipoxygenase that metabolize arachidonate to prostaglandins and leukotrienes (Schievella et al., 1995; Glover et al., 1995). Although these data are compelling, the most definitive evidence for the central role of $cPLA_2$ in eicosanoid and PAF production came from mice made deficient in $cPLA_2$ through homologous recombination (Uozumi et al., 1997; Bonventre et al., 1997). Peritoneal macrophages derived from these animals failed to make leukotrienes, prostaglandins, or PAF. The $cPLA_2$ deficient mice have also been informative of the role of $cPLA_2$ in disease, since these mice are resistant to bronchial hyperreactivity in an anaphylaxis model used to mimic asthma (Uozumi et al., 1997). Thus, despite the size of the phospholipase A_2 superfamily, $cPLA_2$ is essential for prostaglandin, leukotriene, and PAF production.

Clark, J. D., Lin, L.-L., Kriz, R. W., Ramesha, C. S., Sultzman, L. A., Lin, A. Y., Milona, N., and Knopf, J. L. (1991). A novel arachidonic acid-selective cytosolic PLA_2 contains a Ca^{2+}-dependent translocation domain with homology to PKC and GAP. Cell *65*,

1043-1051. Hanel, A. M., and Gelb, M. H. (1993). Processive interfacial catalysis by mammalian 85-kilodalton phospholipase A_2 enzymes on product-containing vesicles: application to the determination of substrate preferences. Biochemistry *32*, 5949-5958.

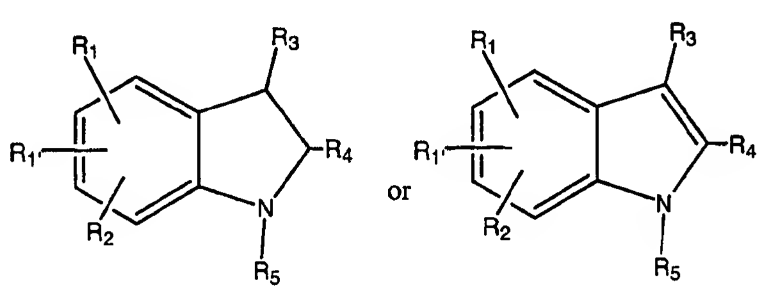
Lin, L.-L., Lin, A. Y., and DeWitt, D. L. (1992a) IL-1 _ induces the accumulation of cPLA2 and the release of PGE_2 in human fibroblasts. J. Biol. Chem. *267*, 23451-23454. Lin, L.-L., Lin, A. Y., and Knopf, J. L. (1992b) Cytosolic phospholipase A_2 is coupled to hormonally regulated release of arachidonic acid. Proc. Natl. Acad. Sci. USA *89*, 6147-6151. Lin, L.-L., Wartmann, M., Lin, A. Y., Knopf, J. L., Seth, A., and Davis, R. J. (1993) $cPLA_2$ is phosphorylated and activated by MAP kinase. Cell *72*, 269-278.

Glover, S., de Carvalho, M., Bayburt, T., Jonas, M., Chi, E., Leslie, E., and Gelb, M. (1995) Translocation of the 85-kDa phospholipase A_2 from cytosol to the nuclear envelope in rat basophilic leukemia cells stimulated with calcium ionophore or IgE/antigen. J. Biol. Chem. *270*, 15359-15367. Schievella, A. R., Regier, M. K., Smith, W. L., and Lin, L.-L. (1995). Calcium-mediated translocation of cytosolic phospholipase A_2 to the nuclear envelope and endoplasmic reticulum. J. Biol. Chem. *270*, 30749-30754.

Uozumi, N., Kume, K., Nagase, T., Nakatani, N., Ishii, S., Tashiro, F., Komagata, Y., Maki, K., Ikuta, K., Ouchi, Y., Miyazaki, J-i., & Shimizu, T. (1997). Role of cytosolic phospholipase A_2 in allergic response and parturition. Nature *390*, 618-622. Bonventre, J. V., Huang, Z., Reza Taheri, M., O'Leary, E., Li, E., Moskowitz, M. A., and Sapirstein, A. (1997) Reduced fertility and postischaemic brain injury in mice deficient in cytosolic phospholipase A_2. Nature *390*, 622-625.

Summary of the Invention

Compounds of this invention have the following formulae:



wherein:

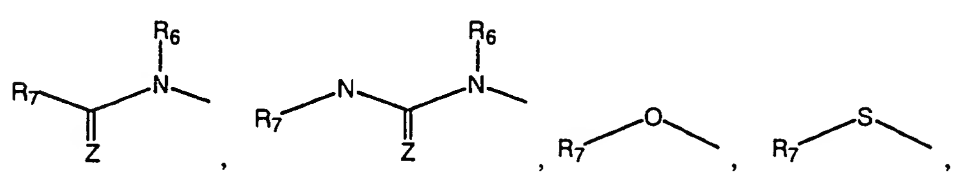
R_1 and $R_{1'}$ are independently selected from H, halogen, $-CF_3$, -OH, $-C_1-C_{10}$ alkyl, preferably $-C_1-C_6$ alkyl, $-S-C_1-C_{10}$ alkyl, preferably $-S-C_1-C_6$ alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CN, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, -S-phenyl, benzyl, -O-benzyl, -S-benzyl; or a ring moiety of the groups a), b) or c), below, directly bonded to the indole ring or bonded to the indole ring by a -S-, -O- or $-(CH_2)_n-$ bridge;

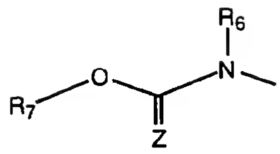
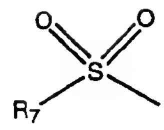
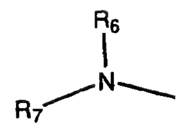
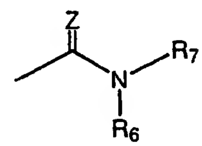
a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, isothiazole, isoxazole, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazole, pyrazoline, imidazole, tetrazole, oxathiazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, $-CF_3$; or

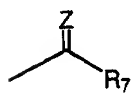
b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyran, pyridine, pyrazine, pyrimidine, pyridazine, piperidine, piperazine, tetrazine, thiazine, thiadizine, oxazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

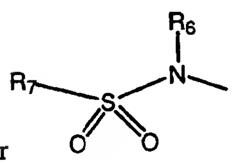
c) a bicyclic ring moiety optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, indolizine, indazole, quinoline, isoquinoline, quinolizine, quinazoline, cinnoline, phthalazine, or napthyridine, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

d) a moiety of the formulae:



, , , ,

,

or ;

Z is O or S;

R_6 is selected from the relevant members of the group H, $-CF_3$, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, phenyl, -O-phenyl, -S-phenyl, benzyl, -O-benzyl, or -S-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$, or -OH;

R_7 is selected from the relevant members of the group -OH, $-CF_3$, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NH_2$, $-(CH_2)_n$-NH_2, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, $-(CH_2)_n$-NH-(C_1-C_6 alkyl), $-(CH_2)_n$-N-(C_1-C_6 alkyl)$_2$, phenyl, -O-phenyl, benzyl, or -O-benzyl; or

a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, isothiazole, isoxazole, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazole, pyrazoline, imidazole, tetrazole, oxathiazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyran, pyridine, pyrazine, pyrimidine,

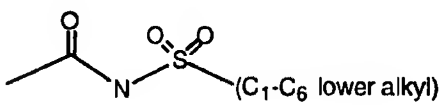
pyridazine, piperidine, piperazine, tetrazine, thiazine, thiadizine, oxazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH; or

c) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, indolizine, indazole, quinoline, isoquinoline, quinolizine, quinazoline, cinnoline, phthalazine, or napthyridine, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH;

n is an integer from 0 to 3;

R_2 is selected from H, halogen, -CN, -CHO, -CF_3, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, -NO_2, -NH_2, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -(CH_2)$_n$-C(O)-COOH, -(CH_2)$_n$-COOH, -CH=CH-COOH, -(CH_2)$_n$-tetrazole,



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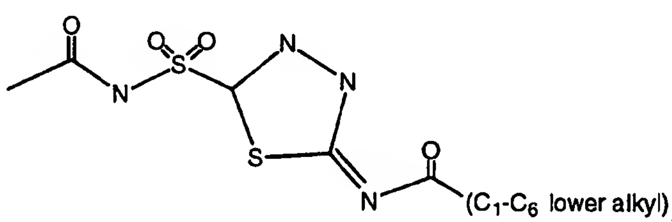

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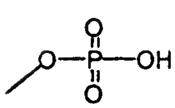

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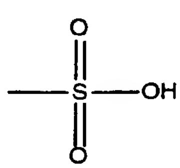
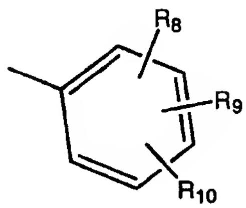


or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$,$-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^1 is selected from the group of -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,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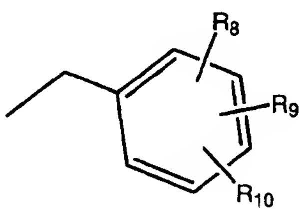
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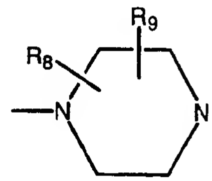
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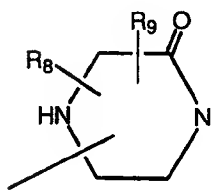
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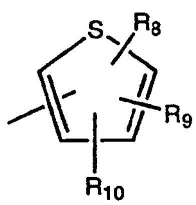
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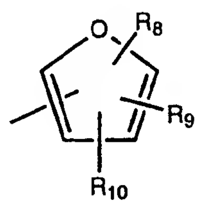
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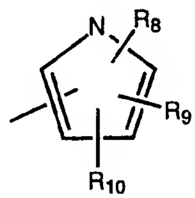
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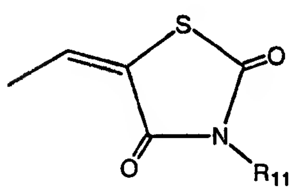
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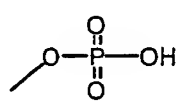
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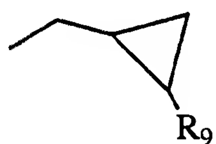
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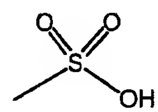

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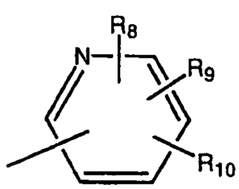
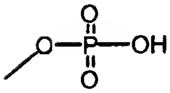
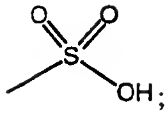
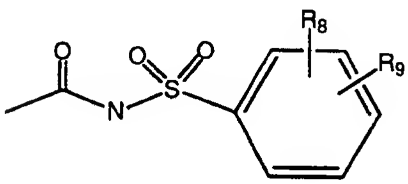
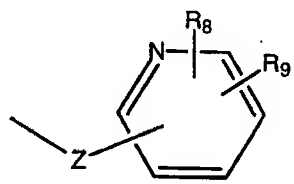


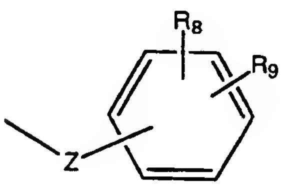
R_8, in each appearance, is independently selected from H, -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,

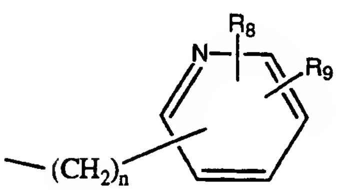
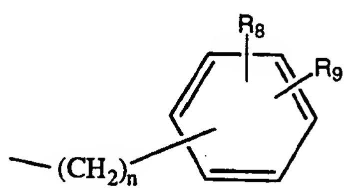
 ,or  ;

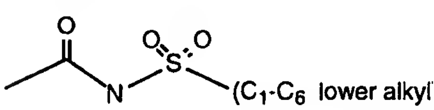
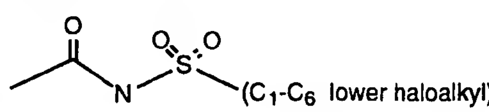
R_9 is selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -O-$(CH_2)_n$-COOH, -O-CH_2-C=C-COOH, -O-C=C-CH_2-COOH, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$, -N-C(O)-$(CH_2)_n$-COOH, -N-SO_2-$(CH_2)_n$-COOH, -C(O)-N-$(CH_2)_n$-COOH;

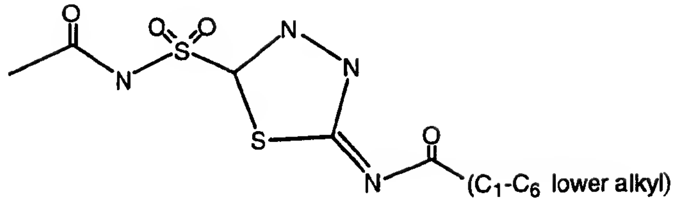
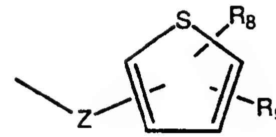
R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -O-(C_1-C_6 alkyl)-$(OH)_n$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$, -N-C(O)-N-(C_1-C_6 alkyl)-$(OH)_2$,

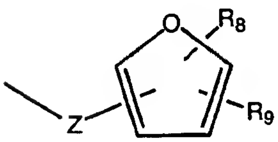
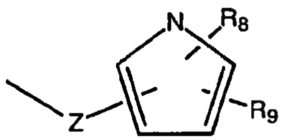
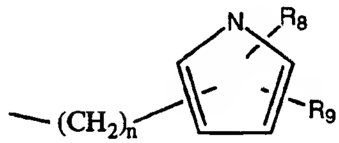
 , 

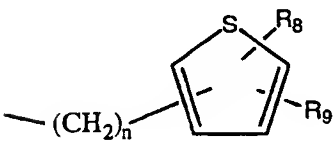
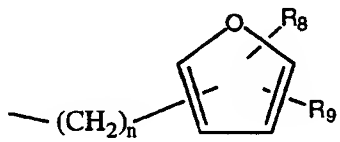
 ,

 , 

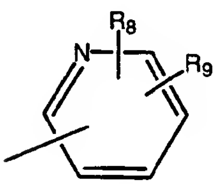
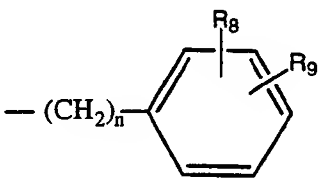
 ,  ,

,
,

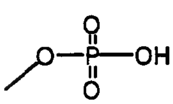
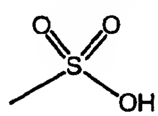
,
,
,

, or
;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, -CF_3, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH,

,
;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:

,

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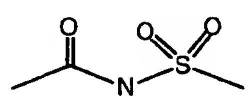
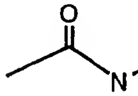
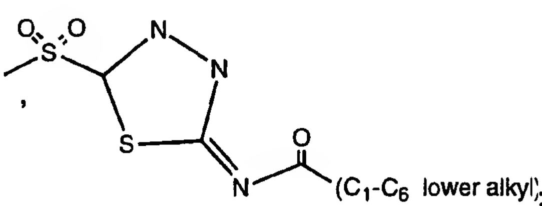
,

,
;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, -C_1-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$, C(O)C(O)X;
where X is O or N

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, isothiazole, isoxazole, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazole, pyrazoline, imidazole, tetrazole, oxathiazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

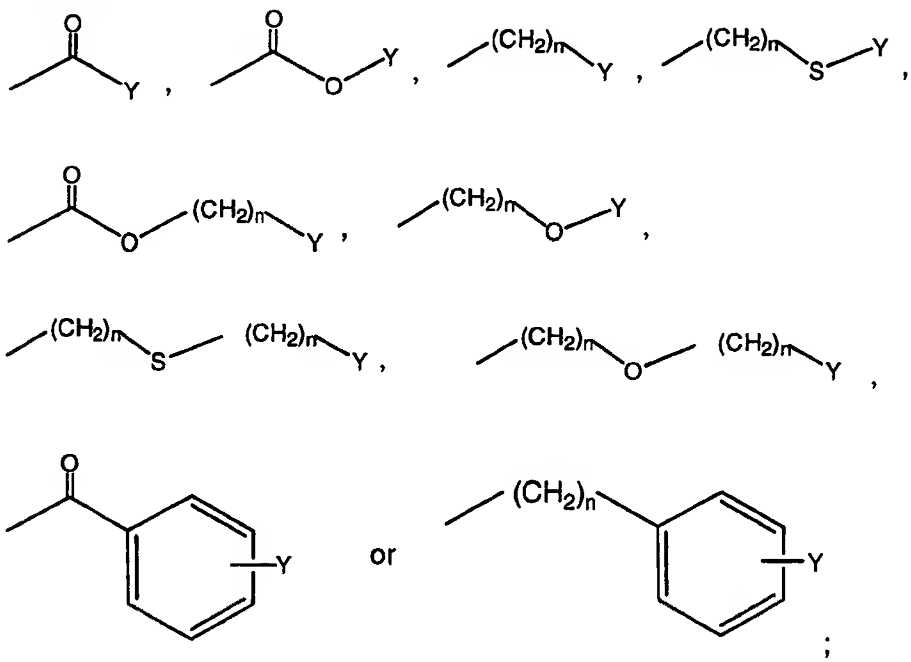
c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyran, pyridine, pyrazine, pyrimidine, pyridazine, piperidine, piperazine, tetrazine, thiazine, thiadizine, oxazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, indolizine, indazole, quinoline, isoquinoline, quinolizine, quinazoline, cinnoline, phthalazine, or napthyridine, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents

selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_{10} cycloalkyl, $-(CH_2)_n$-S-$(CH_2)_n$-C_3-C_{10} cycloalkyl, $-(CH_2)_n$-O-$(CH_2)_n$-C_3-C_{10} cycloalkyl, or the groups of:

a) $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, $-CH_2$-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2,

Y is C_3-C_6 cycloalkyl, phenyl, biphenyl, each optionally substituted by from 1 to 3 groups selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

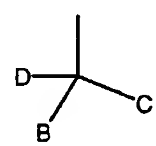
a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, isothiazole, isoxazole, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazole,

pyrazoline, imidazole, tetrazole, oxathiazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, $-CF_3$, or by one phenyl ring, the phenyl ring being optionally substituted by by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, $-CF_3$; or

b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyran, pyridine, pyrazine, pyrimidine, pyridazine, piperidine, piperazine, tetrazine, thiazine, thiadizine, oxazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

c) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, indolizine, indazole, quinoline, isoquinoline, quinolizine, quinazoline, cinnoline, phthalazine, or napthyridine, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

d) a moiety of the formulae $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



wherein

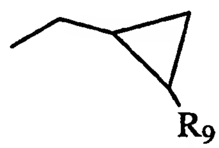
D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-CF_3$ or $-(CH_2)_n-CF_3$;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-N(C_1$-$C_6)_2$, $-NH(C_1$-$C_6)$, $-N-C(O)-(C_1$-$C_6)$, $-NO_2$, or by a 5- or 6-membered heterocyclic or heteroaromatic ring containing 1 or 2 heteroatoms selected from O, N or S, such as, for example, morpholino;

or a pharmaceutically acceptable salt thereof.

One group of compounds within this invention are those in which the indole or indoline 2-position (R_4) is substituted only by hydrogen and the substituents at the other indole or indoline positions are as described above.

Another R_3 is $-L^1-M^1$, wherein L^1 is as defined above, more preferably wherein L^1 is a chemical bond, and M^1 is the moiety:

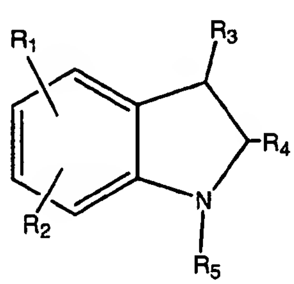


and R_9 is as defined in the broad genus above.

Another group of this invention comprises compounds in which R_2 and R_4 are hydrogen and the groups at R_1, $R_{1'}$, R_3, and R_5 are as defined above. Within this group are two further preferred groups. In the first, R_1 is in the indole or indoline 5 position and in the second R_1 is in the indole or indoline 6 position.

In a further preferred group herein, R_1 is in the indole or indoline 5-position and is benzyloxy, R_2 and R_4 are hydrogen and R_3 and R_5 are as defined above.

Among the more preferred compounds of this invention are those of the following formulae:



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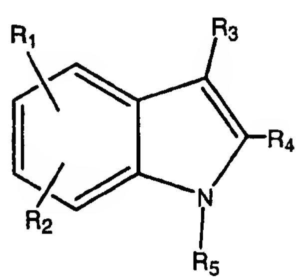
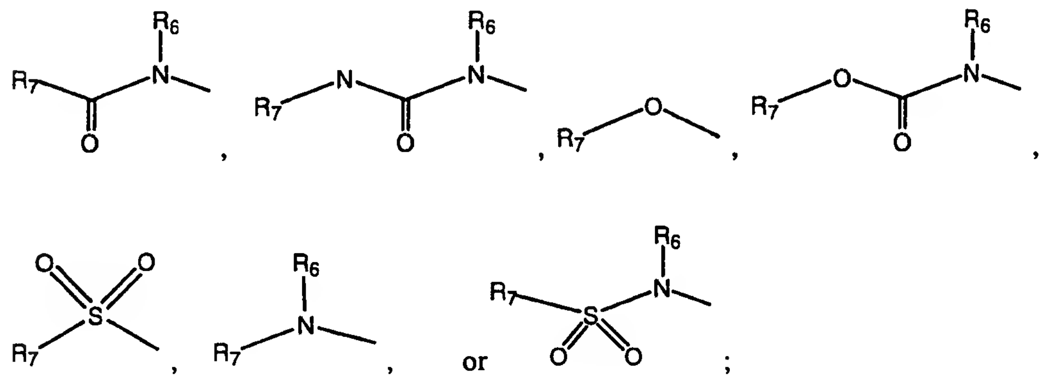


wherein:

R_1 is selected from H, halogen, $-CF_3$, -OH, $-C_1-C_{10}$ alkyl, preferably $-C_1-C_6$ alkyl, -S-C_1-C_{10} alkyl, preferably -S-C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CN, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, -S-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

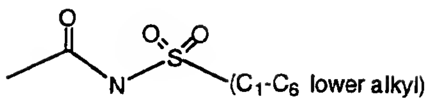


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, $-CF_3$, or -OH;

R_7 is selected from -OH, $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl and thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, -CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, $-CF_3$, -OH, $-C_1-C_{10}$ alkyl, preferably $-C_1-C_6$ alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_n$-tetrazole,



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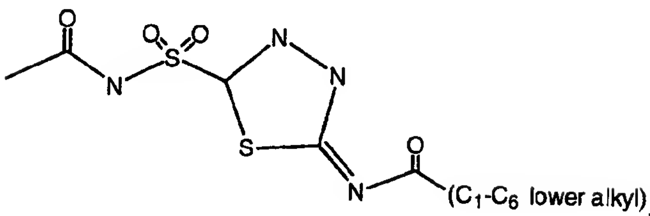

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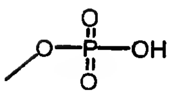

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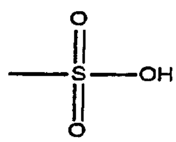
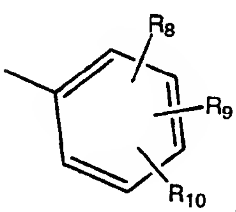


or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, $-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^1 is selected from the group of -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,



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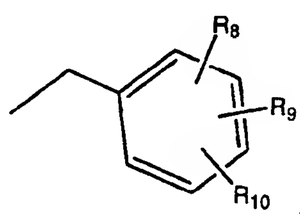

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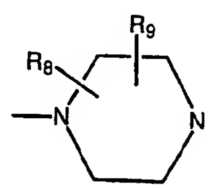

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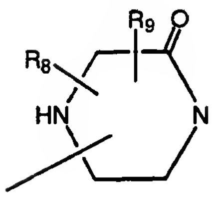
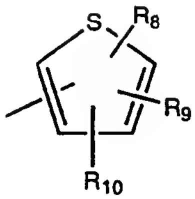
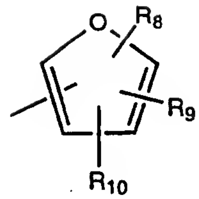
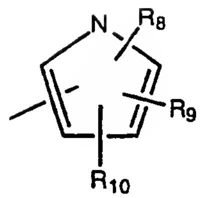
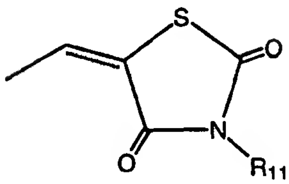
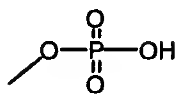
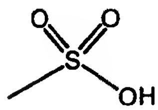
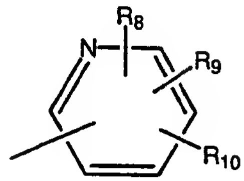
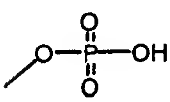
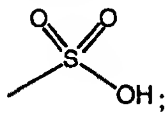
, , , ,

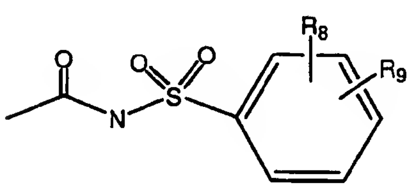
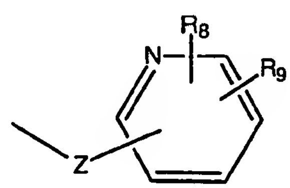
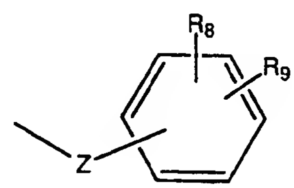
, ,  or 

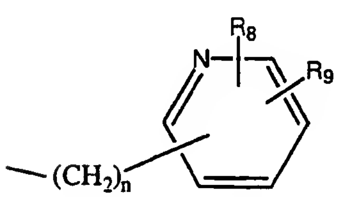
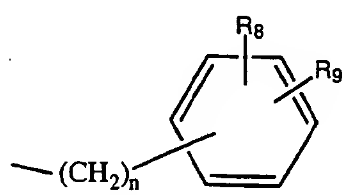
R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

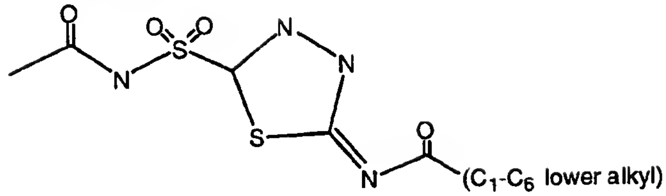
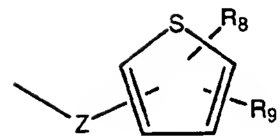
,or ;

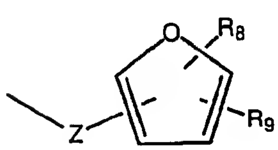
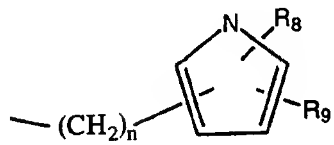
R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), or -N(C_1-C_6 alkyl$)_2$;

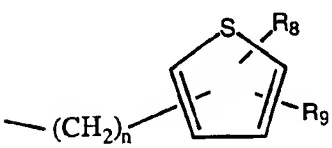
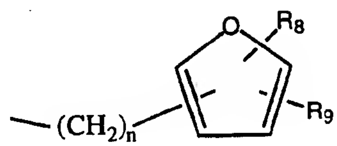
R_{10} is selected from the group of H, halogen, -CF_3, -OH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$,

, , ,

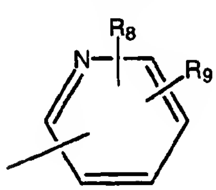
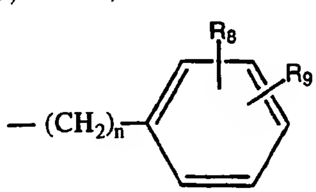
, ,

, ,

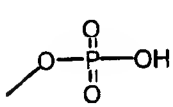
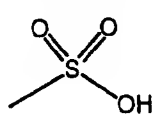
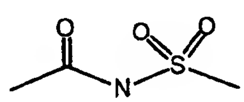
,  ,

, or ;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,

, ;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:

,  or ;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2$-M^2:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^2 is selected from the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

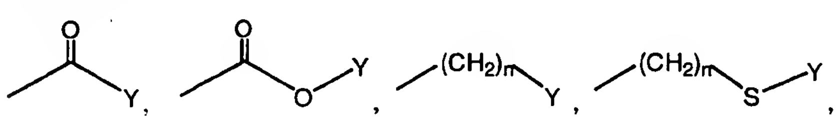
a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

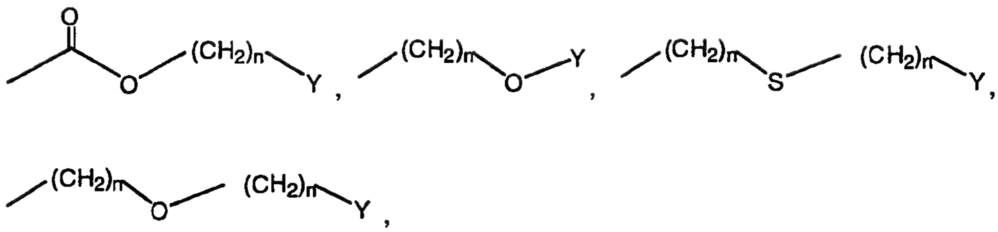
b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to pyridine, pyrimidine, piperidine, piperazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

c) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, indole, indoline, napthalene, purine, or quinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n-C_3-C_{10}$ cycloalkyl,
$-(CH_2)_n-S-(CH_2)_n-C_3-C_{10}$ cycloalkyl, $-(CH_2)_n-O-(CH_2)_n-C_3-C_{10}$ cycloalkyl, or the groups of:

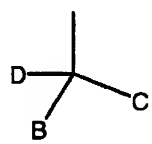
a) $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, $-CH_2$-phenyl-C(O)-benzothiazole or a moiety of the formulae:





wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole and pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, -CN, $-NH_2$, $-NO_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O, preferably S or O; or

b) a moiety of the formulae $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-CF_3$ or $-(CH_2)_n-CF_3$;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$ or $-NO_2$;
or a pharmaceutically acceptable salt thereof.

One group of compounds within this invention are those in which the indole or indoline 2-position (R_4) is substituted only by hydrogen and the substituents at the other indole or indoline positions are as described above.

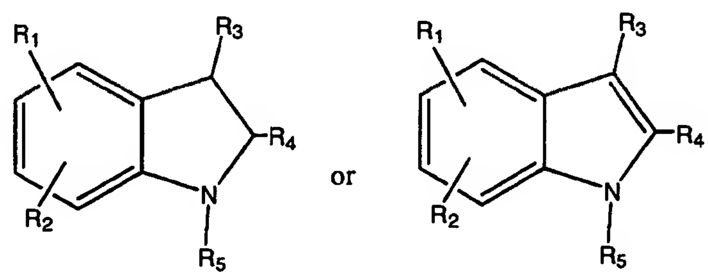
In an another preferred group of this invention R_1 is in the indole or indoline 5 or 6 position and is cyclopentylcarboxamide or cyclopentyloxycarbonylamino, R_2 and R_4 are hydrogen, and R_3 and R_5 are as defined above.

A further preferred group of this invention consists of R_1 and R_2at the indole or indoline 5 and or 6 position and are each selected from the group consisting of C_1-C_6alkoxy, cyano, sulfonyl and halo, R_2 and R_4 are hydrogen, and R_3 and R_5 are as defined above.

Another group of this invention comprises compounds in which R_2 and R_4 are hydrogen and the groups at R_1, R_3, and R_5 are as defined above. Within this group are two further preferred groups. In the first, R_1 is in the indole or indoline 5 position and in the second R_1 is in the indole or indoline 6 position.

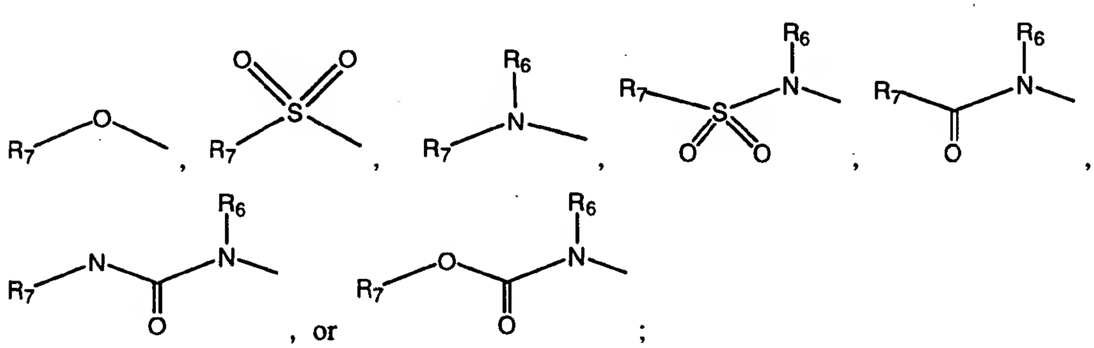
In a further preferred group herein, R_1 is in the indole or indoline 5-position and is benzyloxy, R_2 and R_4 are hydrogen and R_3 and R_5 are as defined above.

A preferred group of compounds of this invention have the following formulae:



wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, CN, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

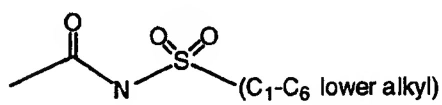


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl and thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



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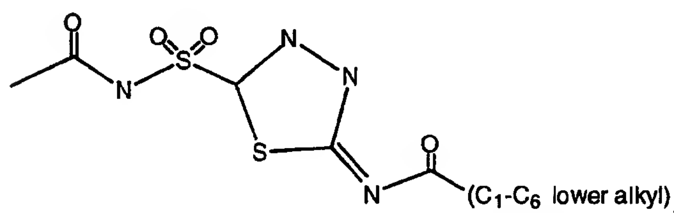

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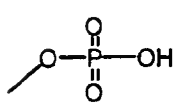

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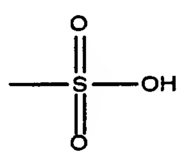
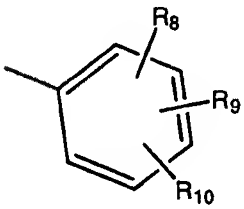


or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-,-$(CH_2)_n$-S-$(CH_2)_n$-,

-C(Z)-N(R_6)-, -C(Z)-N(R_6)-(CH_2)$_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-(CH_2)$_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-(CH_2)$_n$-;

M' is selected from the group of -COOH, -(CH_2)$_n$-COOH, -(CH_2)$_n$-C(O)-COOH, tetrazole,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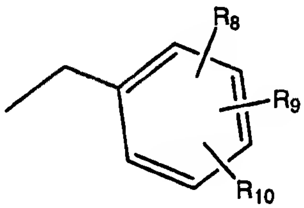
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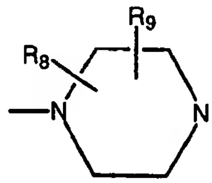
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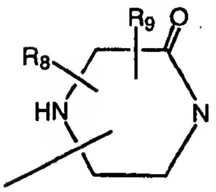
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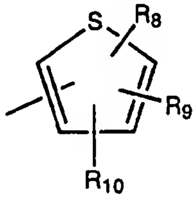
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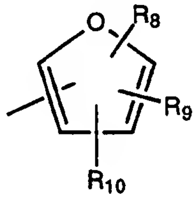
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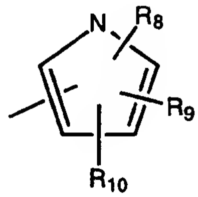
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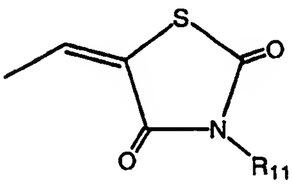
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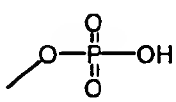
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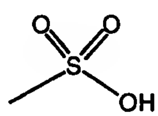
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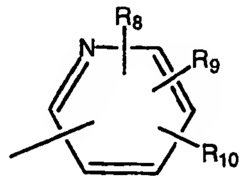
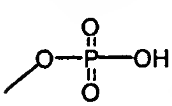


R_8, in each appearance, is independently selected from H, -COOH, -(CH_2)$_n$-COOH, -(CH_2)$_n$-C(O)-COOH, tetrazole,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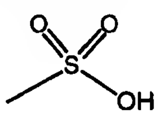
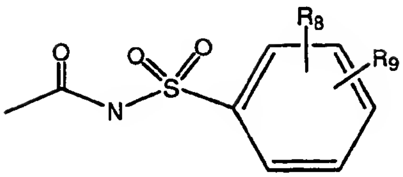

;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -(CH_2)$_n$-COOH, -(CH_2)$_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -(CH_2)$_n$-COOH, -(CH_2)$_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,



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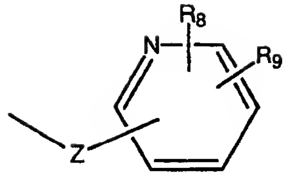

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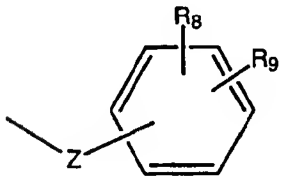

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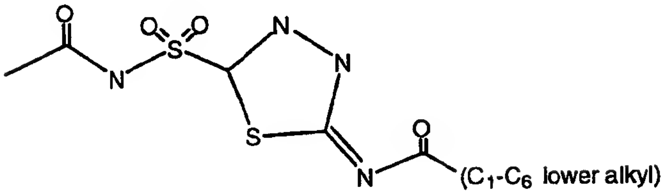

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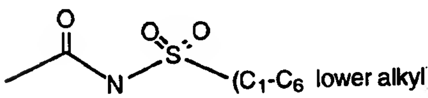

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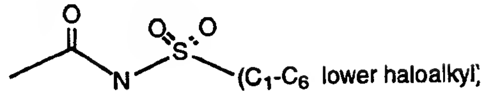
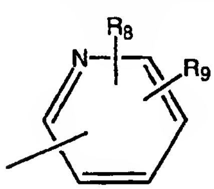


;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,



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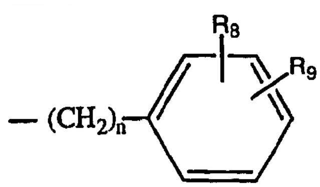
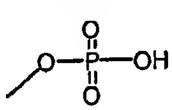


;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae: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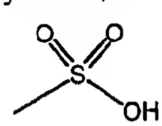
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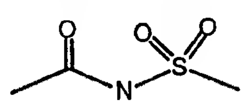

;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, -C_1-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

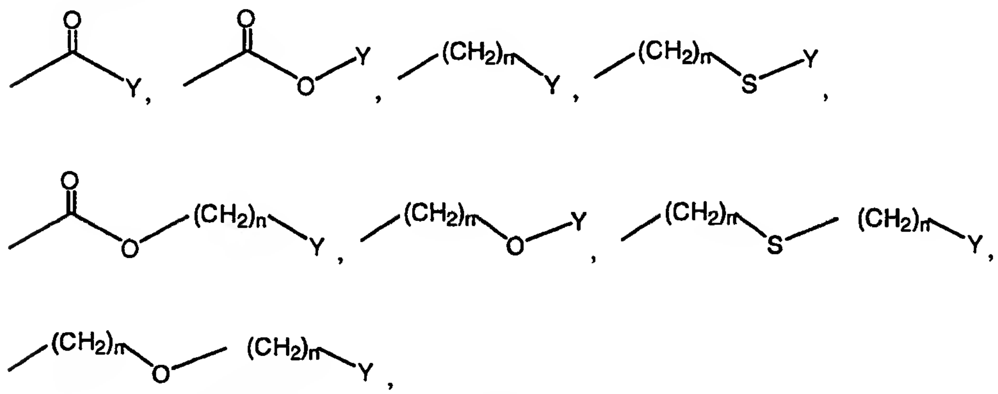
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

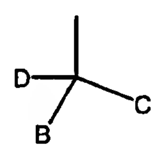
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n-C_3-C_5$ cycloalkyl, $-(CH_2)_n-S-(CH_2)_n-C_3-C_5$ cycloalkyl, $-(CH_2)_n-O-(CH_2)_n-C_3-C_5$ cycloalkyl, or the groups of:

a) -$(CH_2)_n$-phenyl-O-phenyl, -$(CH_2)_n$-phenyl-CH_2-phenyl, -$(CH_2)_n$-O-phenyl-CH_2-phenyl, -$(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, -CH_2-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl benzothiazole or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NO_2, -NH_2 or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O, preferably S or O; or

b) a moiety of the formulae -$(CH_2)_n$-A, -$(CH_2)_n$-S-A, or -$(CH_2)_n$-O-A, wherein A is the moiety:



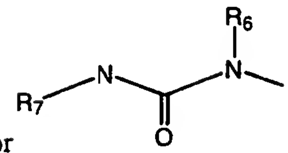
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, -$(CH_2)_n$-CF_3 or -CF_3;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH_2 or -NO_2;
or a pharmaceutically acceptable salt thereof.

A preferred group among the compounds above are those in which the R_1 substitution is at the indole or indoline ring's 5-position and the other substituents are as defined above.

Another preferred group of this invention are those of the formulae:



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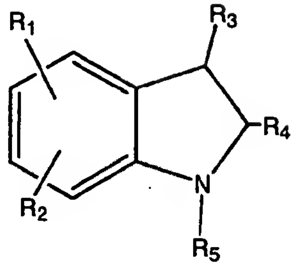
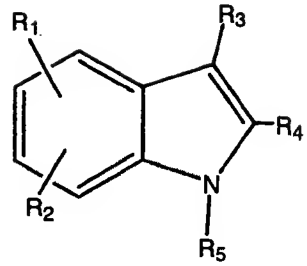
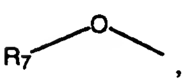
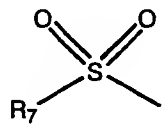
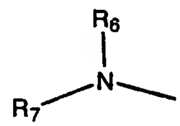
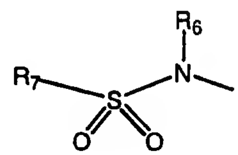
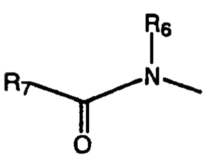
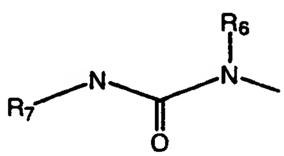
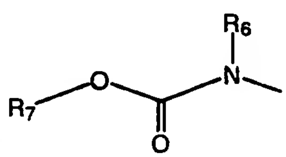
 or 

wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

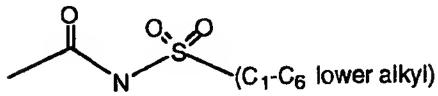
, , , , , , or ;

R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl or thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, $-NH-C_1-C_6$ alkyl, $-N(C_1-C_6$ alkyl$)_2$, $-N-SO_2-C_1-C_6$ alkyl, or $-SO_2-C_1-C_6$ alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



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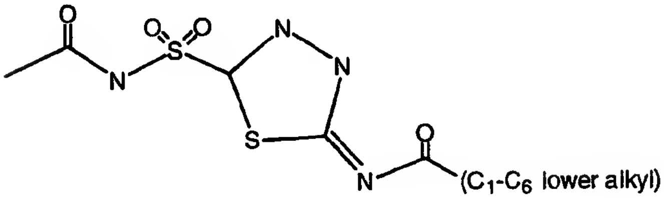

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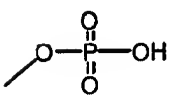
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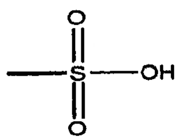
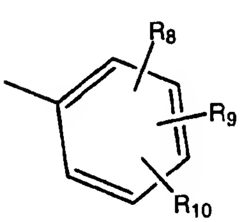


or a moiety selected from the formulae -L^1-M^1;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-,-$(CH_2)_n$-S-$(CH_2)_n$-, -C(Z)-N(R_6)-, -C(Z)-N(R_6)-$(CH_2)_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-$(CH_2)_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-$(CH_2)_n$-;

M^1 is selected from the group of -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,



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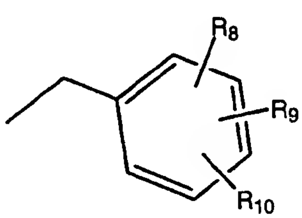

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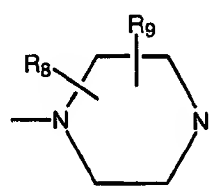

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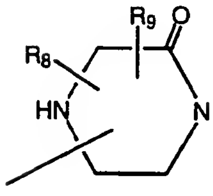
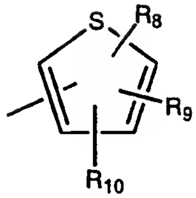
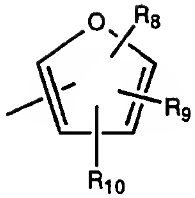
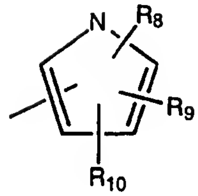
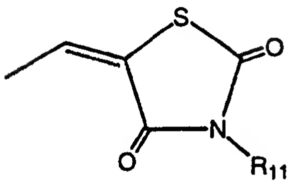
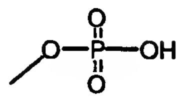
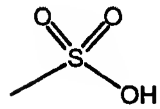
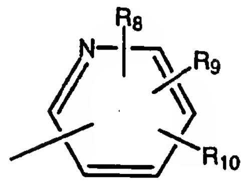
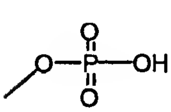
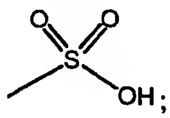
 ,  ,  ,  ,

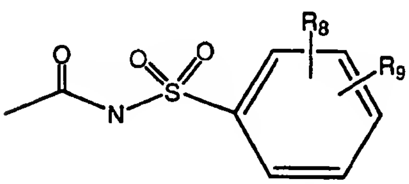
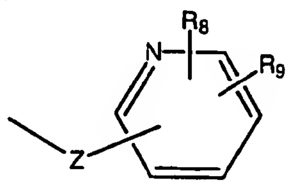
 ,  ,  or 

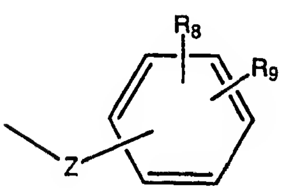
R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

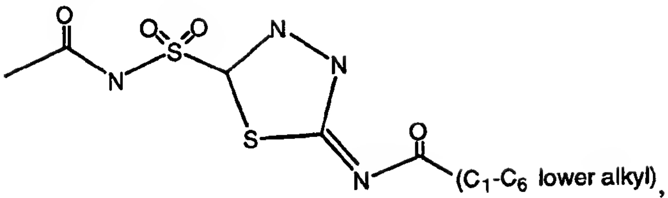
 ,or  ;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$,

 ,  ,

 or



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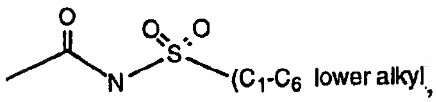

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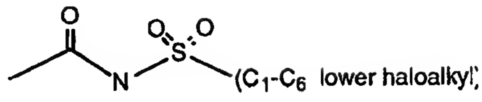
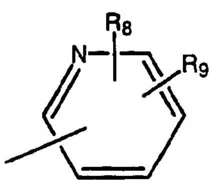


;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,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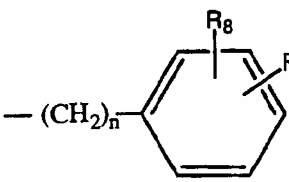
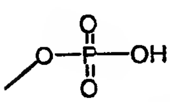

;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae: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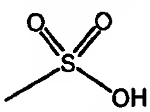
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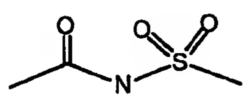

;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n$-C(O)-, $-(CH_2)_n$-C(O)-$(CH_2)_n$-, $-(CH_2)_n$-O-$(CH_2)_n$-, or $-(CH_2)_n$-S-$(CH_2)_n$-;

M^2 is selected from:

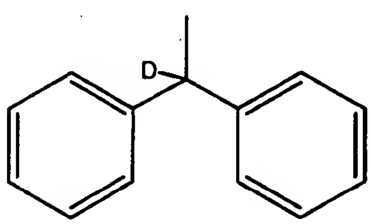
a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl or $--(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A wherein A is selected from :



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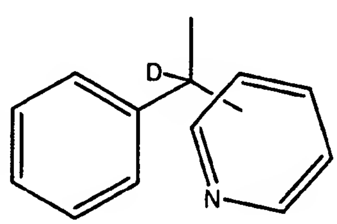

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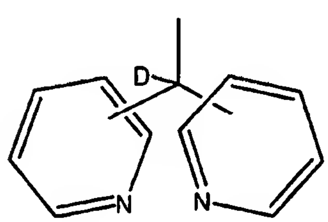

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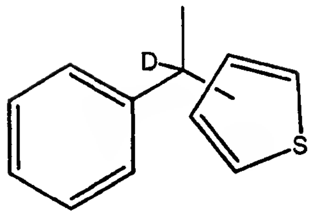
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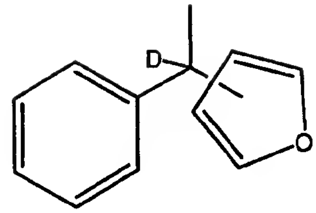
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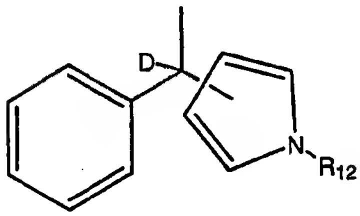
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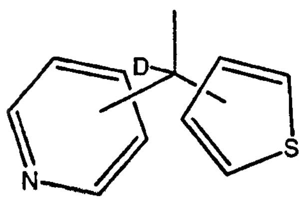
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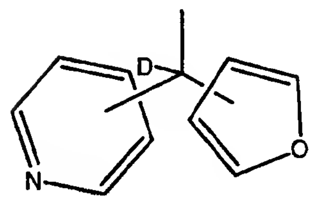
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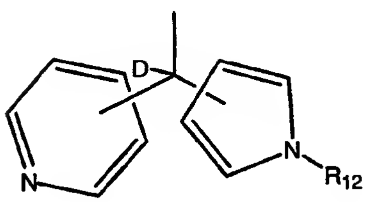
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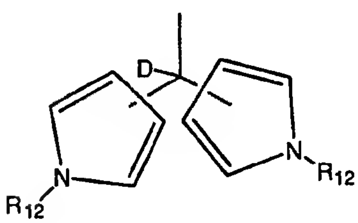
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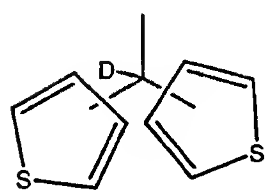
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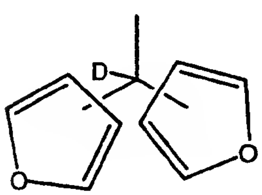
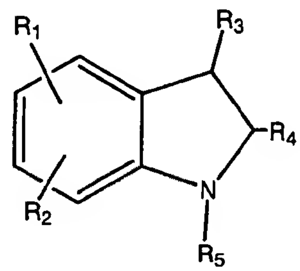

;

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

R_{12} is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

or a pharmaceutically acceptable salt thereof.

Other compounds of this invention have the following formulae:



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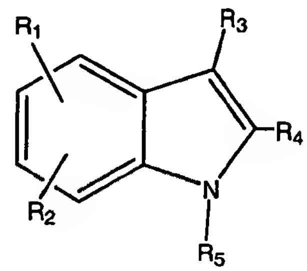
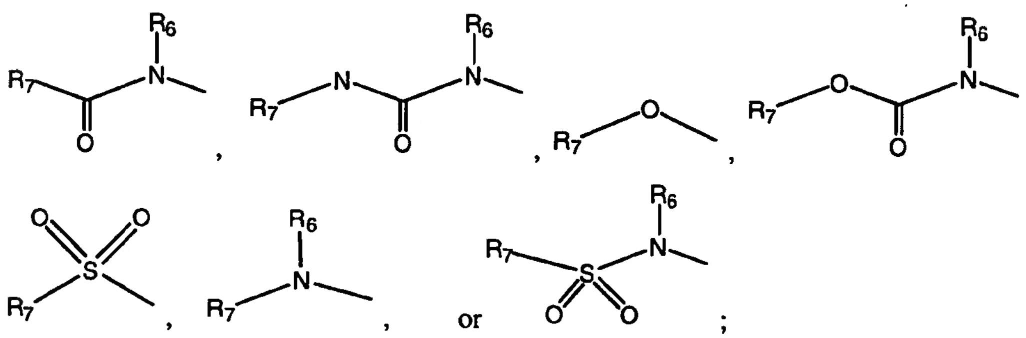


wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

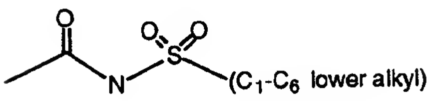


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, pyrazolyl, thiazolyl, -O-phenyl, benzyl or -O-benzyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, $-NH-C_1$-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, $-N-SO_2-C_1$-C_6 alkyl, or $-SO_2-C_1$-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



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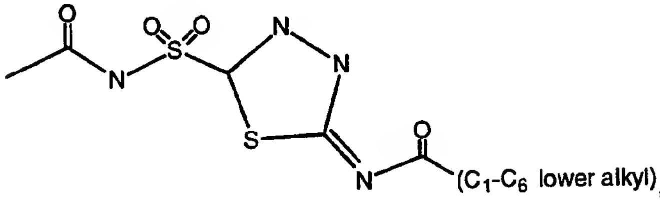

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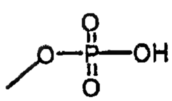

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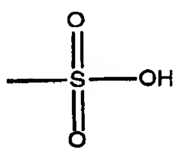
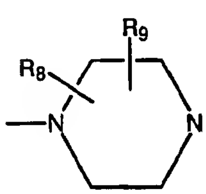


or a moiety selected from the formulae -L^1-M^1 or L^2M^2;

L^1 is a bridging or linking moiety selected from a chemical bond, -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-,-$(CH_2)_n$-S-$(CH_2)_n$-, -C(Z)-N(R_6)-, -C(Z)-N(R_6)-$(CH_2)_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-$(CH_2)_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-$(CH_2)_n$-;

M^1 is selected from the group of -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,



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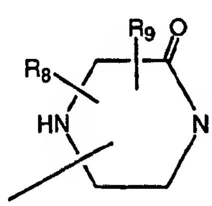

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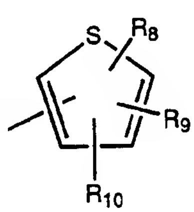

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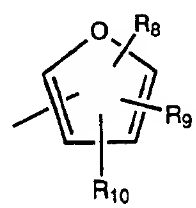

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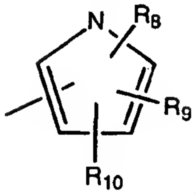
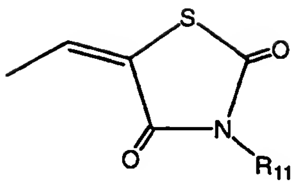
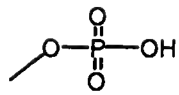
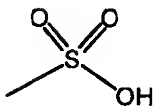
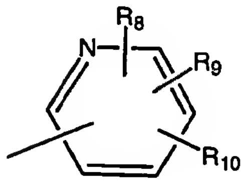
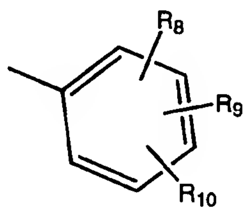
 ,  ,  ,

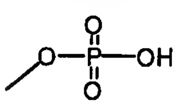
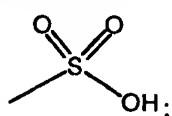
 or 

L^2 is a bridging or linking moiety selected from a chemical bond -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, $-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^2 is the moiety

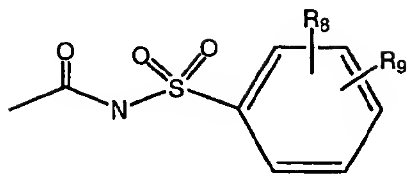
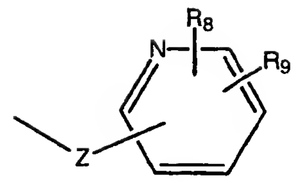
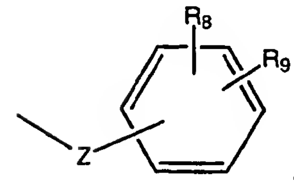
 ;

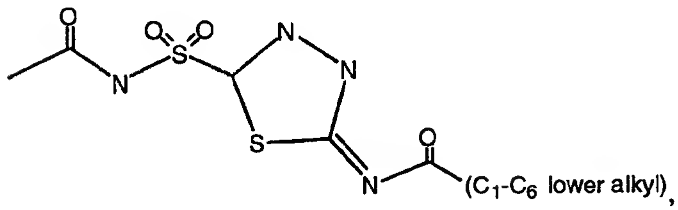
R_8, in each appearance, is independently selected from H, -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,

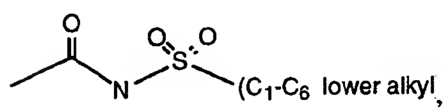
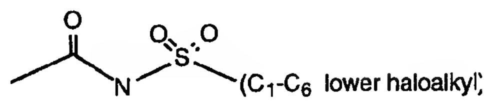
 ,or  ;

R_9 is selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, $-C_1-C_6$ alkyl, $-O-C_1-C_6$ alkyl, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl$)_2$;

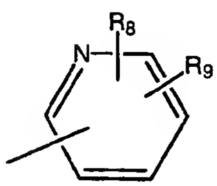
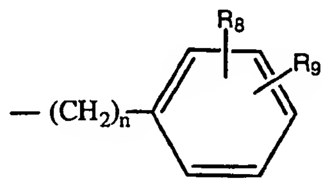
R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, $-C_1-C_6$ alkyl, $-O-C_1-C_6$ alkyl, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl$)_2$,

, ,  or

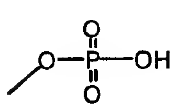
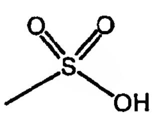
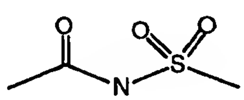
,

,  ;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,

,  ;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, L^2, M^2, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:

,  or  ;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^3$-M^3:

L^3 indicates a linking or bridging group of the formulae $-(CH_2)_n$-, -S-, -O-,

-C(O)-, $-(CH_2)_n$-C(O)-, $-(CH_2)_n$-C(O)-$(CH_2)_n$-, $-(CH_2)_n$-O-$(CH_2)_n$-, or $-(CH_2)_n$-S-$(CH_2)_n$-;

M^3 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

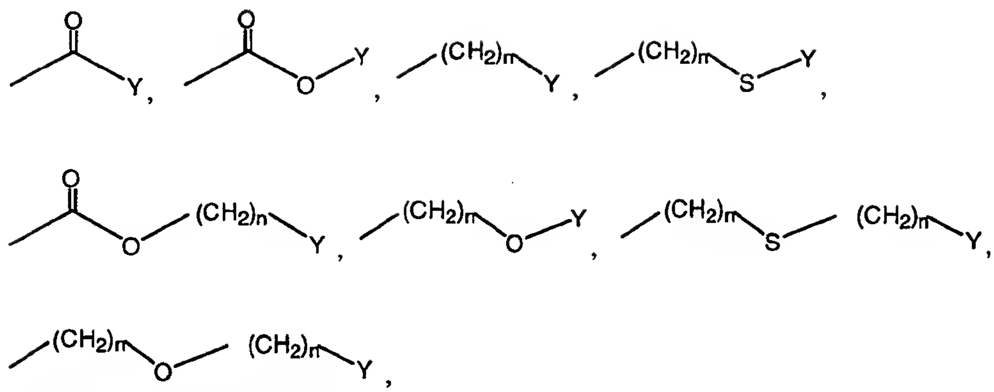
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

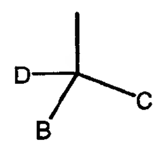
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl, $-(CH_2)_n$-S-$(CH_2)_n$-C_3-C_5 cycloalkyl, $-(CH_2)_n$-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, or the groups of:

a) $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, -CH_2-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole, or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O, preferably S or O; or

b) a moiety of the formulae $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



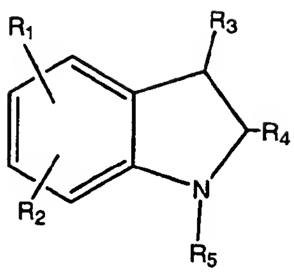
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-CF_3$ or $-(CH_2)_n-CF_3$;

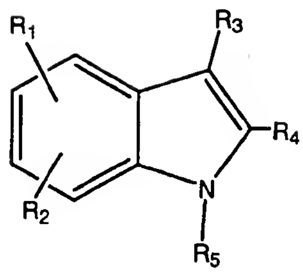
B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$ or $-NO_2$;

or a pharmaceutically acceptable salt thereof.

Another preferred group of this invention are those of the formulae:

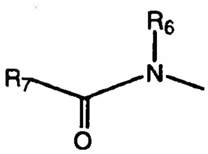


or



wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae: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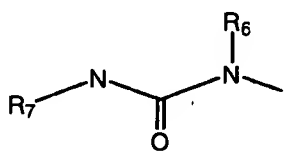
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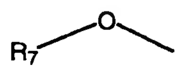
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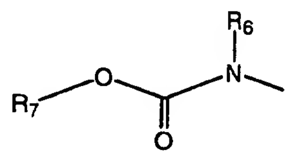
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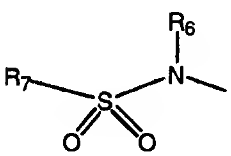
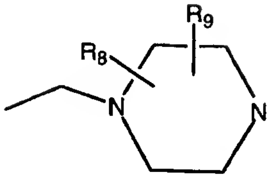
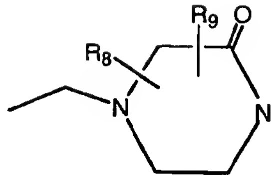
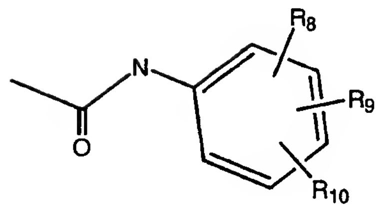
or

;

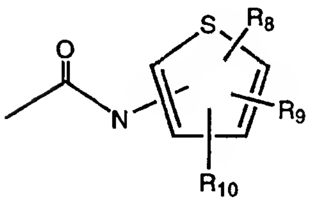
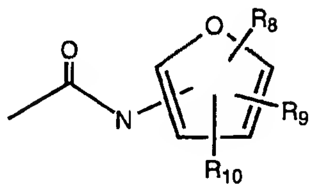
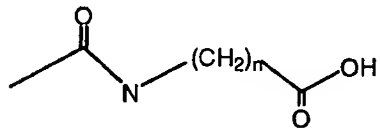
R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

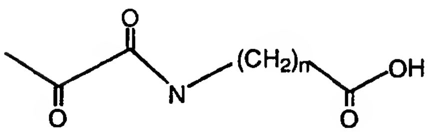
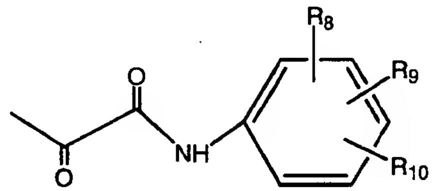
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl and thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

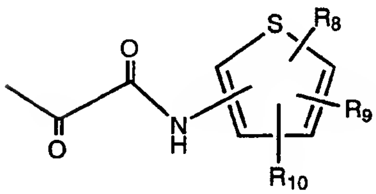
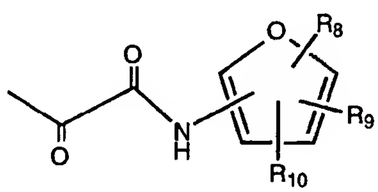
R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, $-NH-C_1$-C_6 alkyl, $-N(C_1$-C_6 alkyl$)_2$, $-N-SO_2-C_1$-C_6 alkyl, or $-SO_2-C_1$-C_6 alkyl;

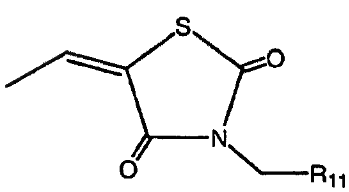
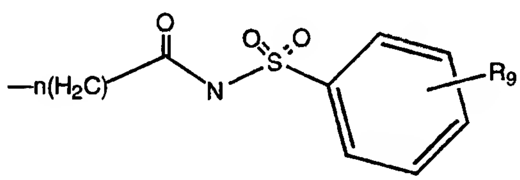
R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_nC(O)NS(O)(O)(C_1$-$C_6$ lower alkyl), $-(CH_2)_NC(O)NS(O)(O)(C_1$-$C_6$ lower haloalkyl),

, , ,

, , ,

, ,

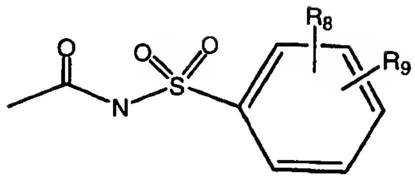
, , or

, ;

R_8 is selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,



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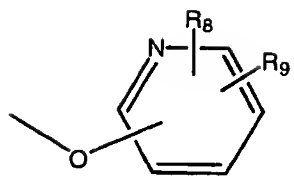

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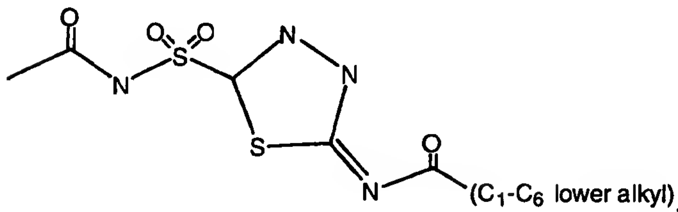

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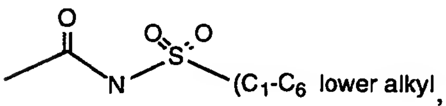

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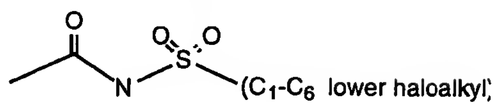
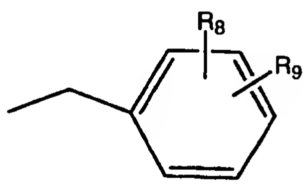


;

R_{11} is selected from H, C_1-C_6 lower alkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, or



;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n$-C(O)-, $-(CH_2)_n$-C(O)-$(CH_2)_n$-, $-(CH_2)_n$-O-$(CH_2)_n$-, or $-(CH_2)_n$-S-$(CH_2)_n$-;

M^2 is selected from:

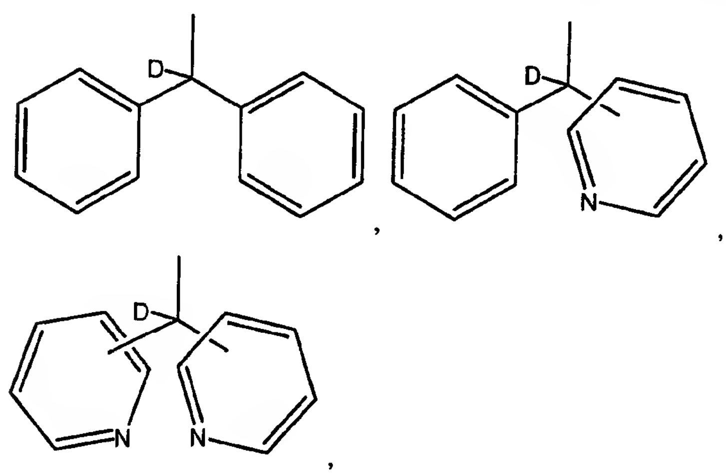
a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

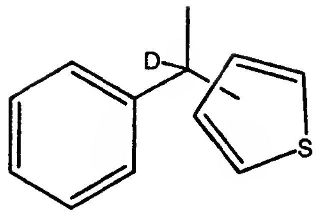
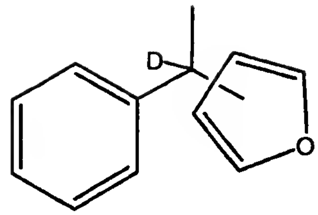
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

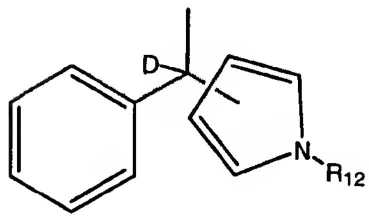
c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH; or

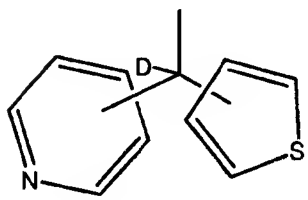
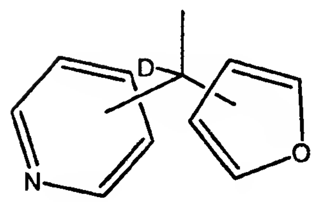
d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

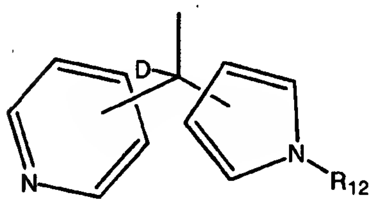
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl or $--(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A wherein A is selected from:

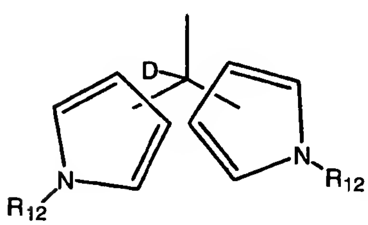
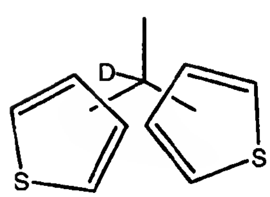
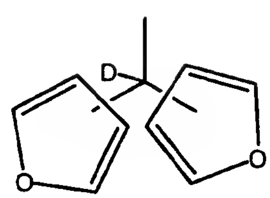


,
,

,

,
,

,

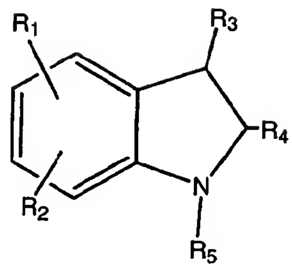
,
, or
;

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

R_{12} is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

or a pharmaceutically acceptable salt thereof.

The compounds of this invention have the following formulae:



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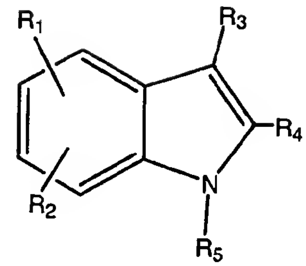
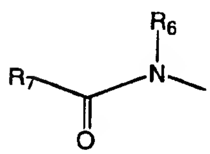


wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:



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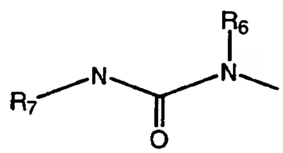

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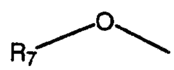

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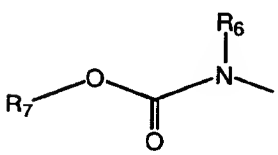

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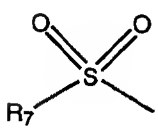

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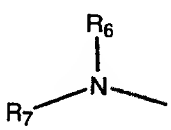

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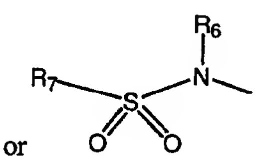


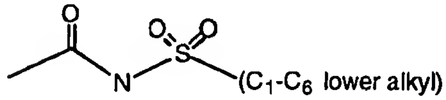
;

R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

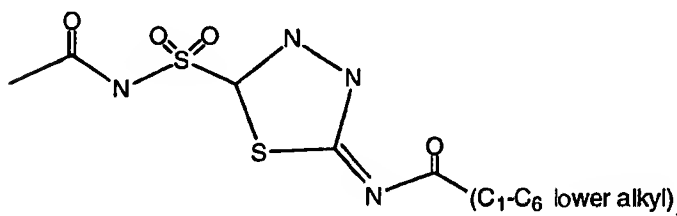
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, pyrazolyl, thiazolyl, -O-phenyl, benzyl or -O-benzyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, -CF_3, -OH, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -CN, -NO_2, -NH_2, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



or



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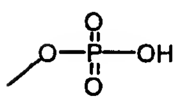

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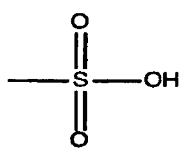
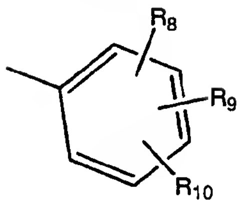
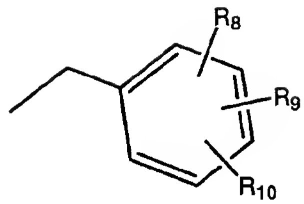
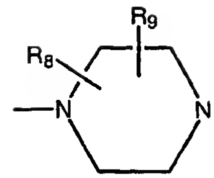
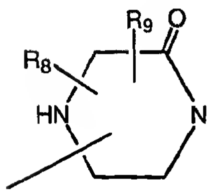
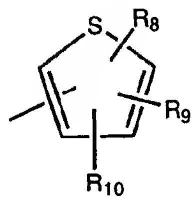
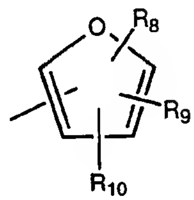
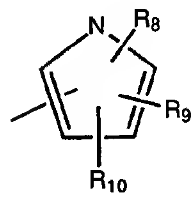


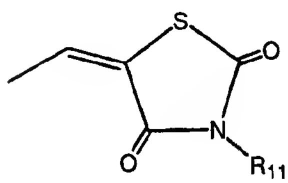
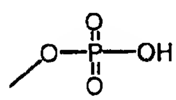
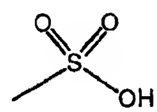
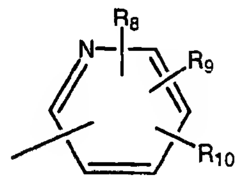
or a moiety selected from the formulae -L^1-M^1;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-,-$(CH_2)_n$-S-$(CH_2)_n$-, -C(Z)-N(R_6)-, -C(Z)-N(R_6)-$(CH_2)_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-$(CH_2)_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-$(CH_2)_n$-;

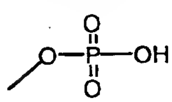
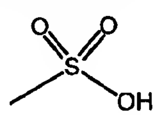
M^1 is selected from the group of -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

, , ,

, , , ,

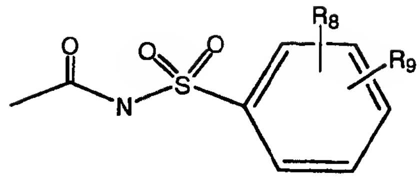
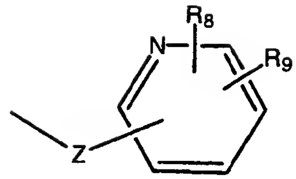
, ,  or 

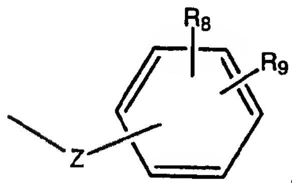
R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

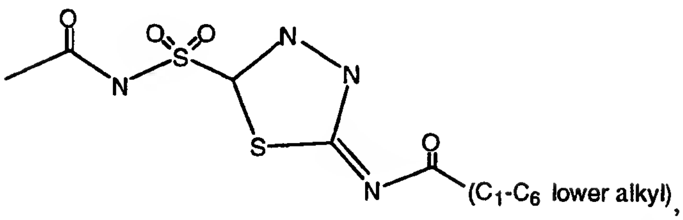
, or ;

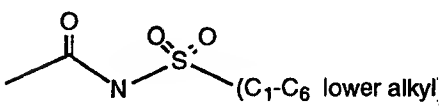
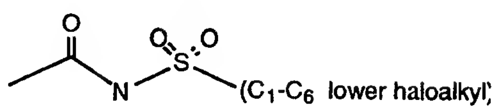
R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,

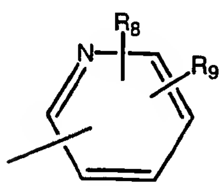
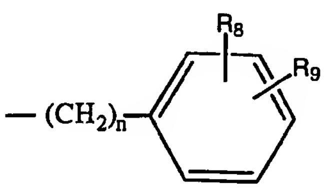
,
,

 or

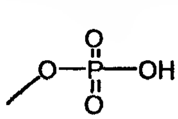
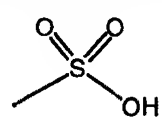
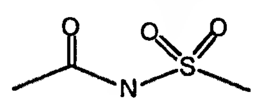
,

, ;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,

, ;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:

,  or ;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2$-M^2:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n$-C(O)-, $-(CH_2)_n$-C(O)-$(CH_2)_n$-, $-(CH_2)_n$-O-$(CH_2)_n$-, or $-(CH_2)_n$-S-$(CH_2)_n$-, -C(O)C(O)X;
where X is O or N,

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

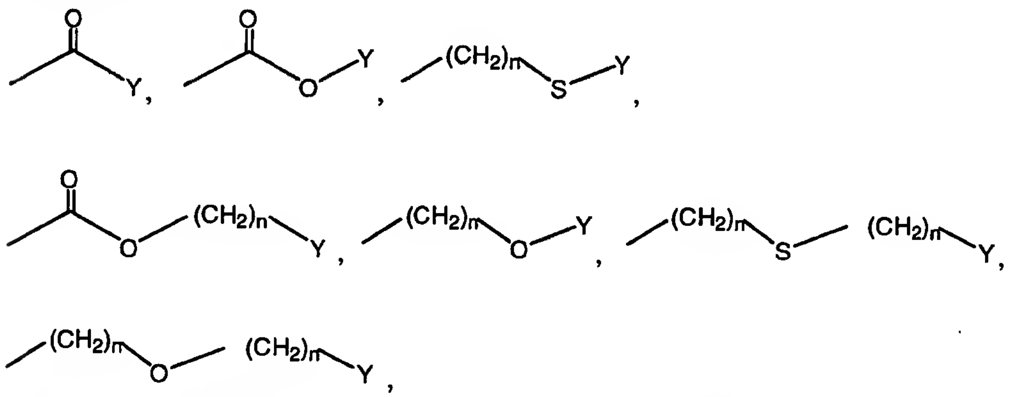
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

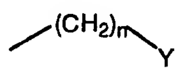
d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

R_5 is selected from $-(CH_2)_n-S-(CH_2)_n-C_3-C_5$ cycloalkyl, $-(CH_2)_n-O-(CH_2)_n-C_3-C_5$ cycloalkyl, or the groups of:

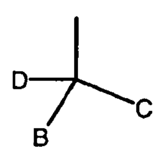
a) $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl)$_2$, $-CH_2$-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O, preferably S or O; or

b) a moiety of the formula  wherein n is an integer from 0 to 3, preferably 1 to 3, more preferably 1 to 2, Y is napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl benzothiazole, or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O, preferably S or O; or

c) a moiety of the formulae $-(CH_2)_n-A$, $-(CH_2)_n-S-A$, or $-(CH_2)_n-O-A$, wherein A is the moiety:



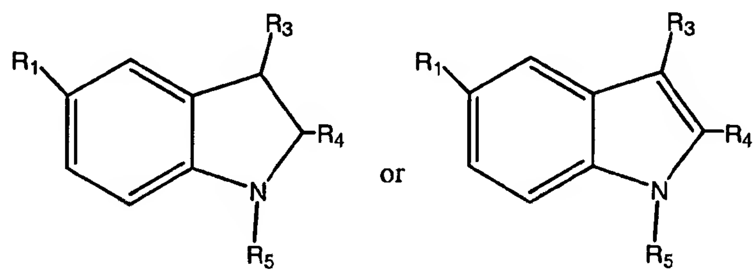
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, -$(CH_2)_n$-CF_3 or -CF_3;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH_2 or -NO_2;
or a pharmaceutically acceptable salt thereof.

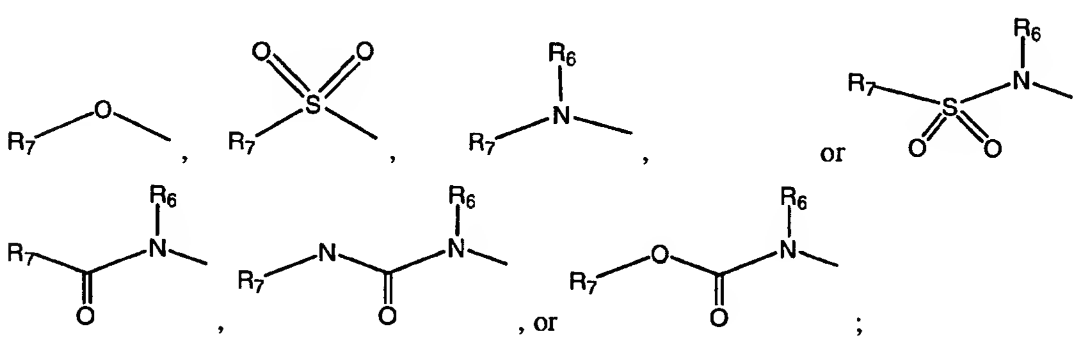
In a further preferred group within the subgenus above, R_1 is benzyloxy and R_4, R_3 and R_5 are as defined above.

Yet another preferred group herein are the compounds of the formulae:



wherein:

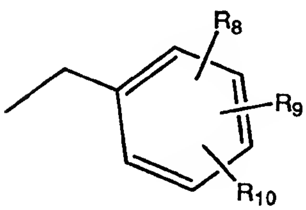
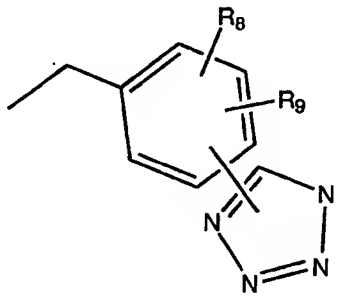
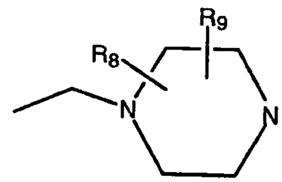
R_1 is selected form H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NO_2, -NH_2, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

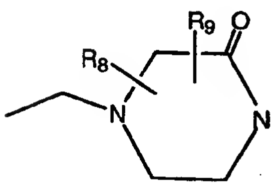
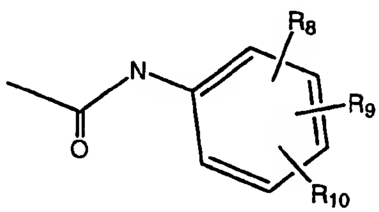
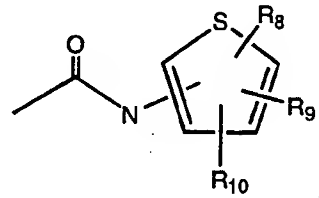


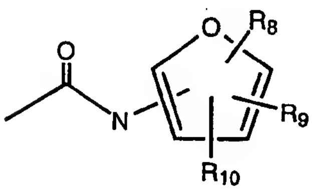
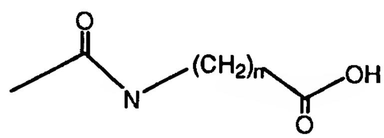
R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH_2, -NO_2, -CF_3, or -OH;

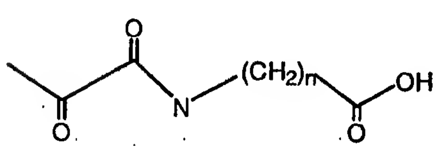
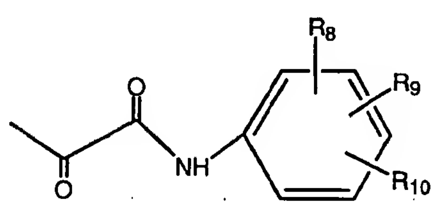
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl or thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

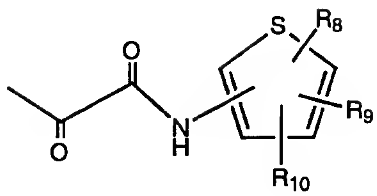
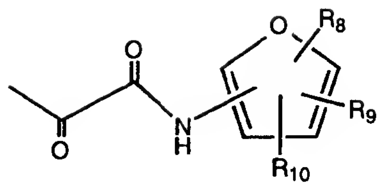
R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_n$C(O)NS(O)(O)(C_1-C_6 lower alkyl), $-(CH_2)_N$C(O)NS(O)(O)(C_1-C_6 lower haloalkyl),

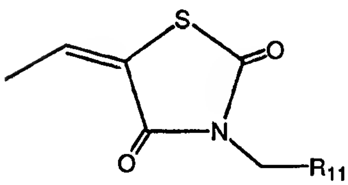
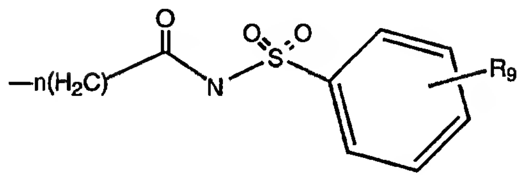
 ,  ,  ,

 ,  ,  ,

 ,  ,

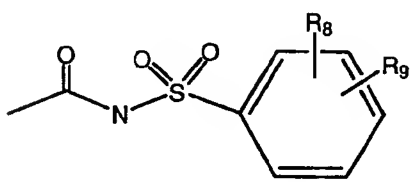
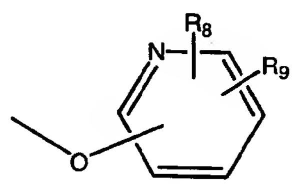
 ,  ,

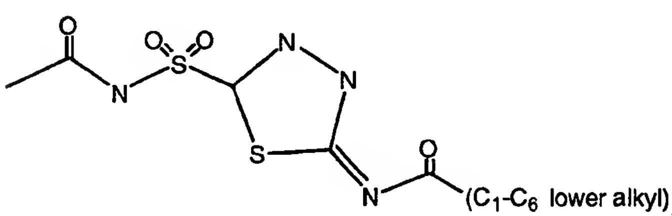
, , or

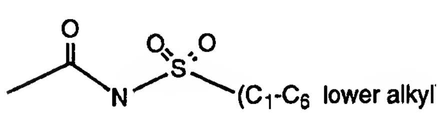
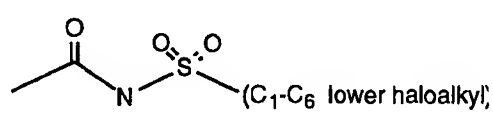
  ;

R_8 and R_9 are independently selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1-C_6$ alkyl, $-O-C_1-C_6$ alkyl, $-NH(C_1-C_6$ alkyl), or $-N(C_1-C_6$ alkyl$)_2$;

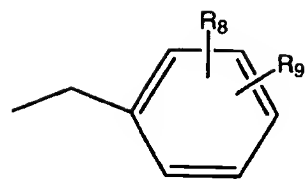
R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1-C_6$ alkyl, $-O-C_1-C_6$ alkyl, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl$)_2$,

, , or

,

,  ;

R_{11} is selected from H, C_1-C_6 lower alkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, or



;

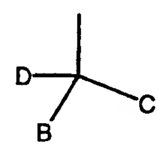
n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or halogen;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl or the groups of:

a) -C(O)-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, $-(CH_2)_n$-phenyl, $-(CH_2)_n$-S-phenyl, $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl)$_2$, -C(O)-O-phenyl, -C(O)-O-benzyl, -C(O)-O-pyridinyl, -C(O)-O-napthyl, $-(CH_2)_n$-S-napthyl, $-(CH_2)_n$-S-pyridinyl, $-(CH_2)_n$-pyridinyl or $-(CH_2)_n$-napthyl, the phenyl, pyridinyl and napthyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, or $-NO_2$; or

b) a moiety of the formula $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

B and C are independently selected from phenyl, pyridinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, or $-NO_2$;
or a pharmaceutically acceptable salt thereof.

__Detailed Description of the Invention__

As used herein, the terms "aryl" and "substituted aryl" are understood to include monocyclic, particularly including five- and six-membered monocyclic, aromatic and heteroaromatic ring moieties and bicyclic aromatic and heteroaromatic ring moieties, particularly including those having from 9 to 10 ring atoms. Among these aryl groups are understood to be phenyl rings, including those found in phenoxy, benzyl, benzyloxy, biphenyl and other such moieties. The aryl and heteroaryl groups of this invention also include the following:

a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, isothiazole, isoxazole, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazole, pyrazoline, imidazole, tetrazole, or oxathiazole; or

b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyran, pyridine, pyrazine, pyrimidine, pyridazine, piperidine, piperazine, tetrazine, thiazine, thiadizine, oxazine, or morpholine; or

c) a bicyclic ring moiety optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, indolizine, indazole, quinoline, isoquinoline, quinolizine, quinazoline, cinnoline, phthalazine, or napthyridine.

The "substituted aryl" groups of this invention include such moieties being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, preferably C_1-C_6 alkyl, C_1-C_{10} alkoxy, preferably C_1-C_6 alkoxy, -CHO, -COOH or esters thereof, -NO_2, -NH_2, -CN, -CF_3 or -OH or combinations thereof, such as -CH_2CF_3, -$NH(CH_3)$, etc.

A preferred subset of these groups, optionally substituted as just described, include moieties formed from benzene, pyridine, napthylene or quinoline rings. A further preferred group includes those of furan, pyrrole, thiophene, pyrimidine, and morpholine rings. A preferred group of bicyclic aromatic groups includes benzofuran, indole, napthalene, and quinoline rings.

The alkyl, alkenyl and alkinyl groups referred to herein indicate such groups having from 1 to 10, preferably 1 to 6 carbon atoms, and may be straight, branched or cyclic. Unless indicated otherwise, it is preferred that these groups be straight or branched. Halogens herein are understood to include F, Cl, Br and I.

As used herein, "phospholipase enzyme activity" means positive activity in an assay for metabolism of phospholipids (preferably one of the assays described in Example 116 below). A compound has "phospholipase enzyme inhibiting activity" when it inhibits the activity of a phospholipase (preferably $cPLA_2$) in any available assay (preferably an assay described below in Example 116 or Example 117) for enzyme activity. In preferred embodiments, a compound has (1) an IC_{50} value of less than about 25 μM, preferably less than about 6 μM, in the LysoPC assay; (2) an IC_{50} value of less than about 50 μM in the vesicle assay; (3) an IC_{50} value of less than about 1 μM in the PMN assay; (4) an IC_{50} value of less than about 15 μM in the Coumarine assay; and/or (5) measurable activity (preferably at least about 5% reduction in edema, more preferably at least about 10% reduction, more preferably at least about 15%, most preferably 20-30%) in the rat carrageenan-induced footpad edema test.

Compounds of the present invention are useful for inhibiting phospholipase enzyme (preferably $cPLA_2$) activity and, therefore, are useful in "treating" (i.e., treating, preventing or ameliorating) inflammatory or inflammation-related responses or conditions (e.g., rheumatoid arthritis, psoriasis, asthma, inflammatory bowel disease, and other diseases mediated by prostaglandins, leukotrienes or PAF) and other conditions, such as osteoporosis, colitis, myelogenous leukemia, diabetes, wasting and atherosclerosis.

The present invention encompasses both pharmaceutical compositions and therapeutic methods of treatment or use which employ compounds of the present invention.

Compounds of the present invention may be used in a pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to a compound or compounds of the present invention and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition may further contain other anti-inflammatory agents. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with compounds of the present invention, or to minimize side effects caused by the compound of the present invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which compounds of the present invention are combined, in addition to other pharmaceutically

acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of an inflammatory response or condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of a compound of the present invention is administered to a mammal having a condition to be treated. Compounds of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing other anti-inflammatory agents, cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more other anti-inflammatory agents, cytokines, lymphokines or other hematopoietic factors, compounds of the present invention may be administered either simultaneously with the other anti-inflammatory agent(s), cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering compounds of the present invention in combination with other anti-inflammatory agent(s), cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of compounds of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, or cutaneous, subcutaneous, or intravenous injection.

When a therapeutically effective amount of compounds of the present invention is administered orally, compounds of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% compound of the present invention, and preferably from about 25 to 90% compound of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of compound of the present invention, and preferably from about 1 to 50% compound of the present invention.

When a therapeutically effective amount of compounds of the present invention is administered by intravenous, cutaneous or subcutaneous injection, compounds of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to compounds of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of compound(s) of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of compound of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of compound of the present invention and observe the patient's response. Larger doses of compounds of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.1 μg to about 100 mg (preferably about .1 mg to about 50

mg, more preferably about 1 mg to about 2 mg) of compound of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the compounds of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

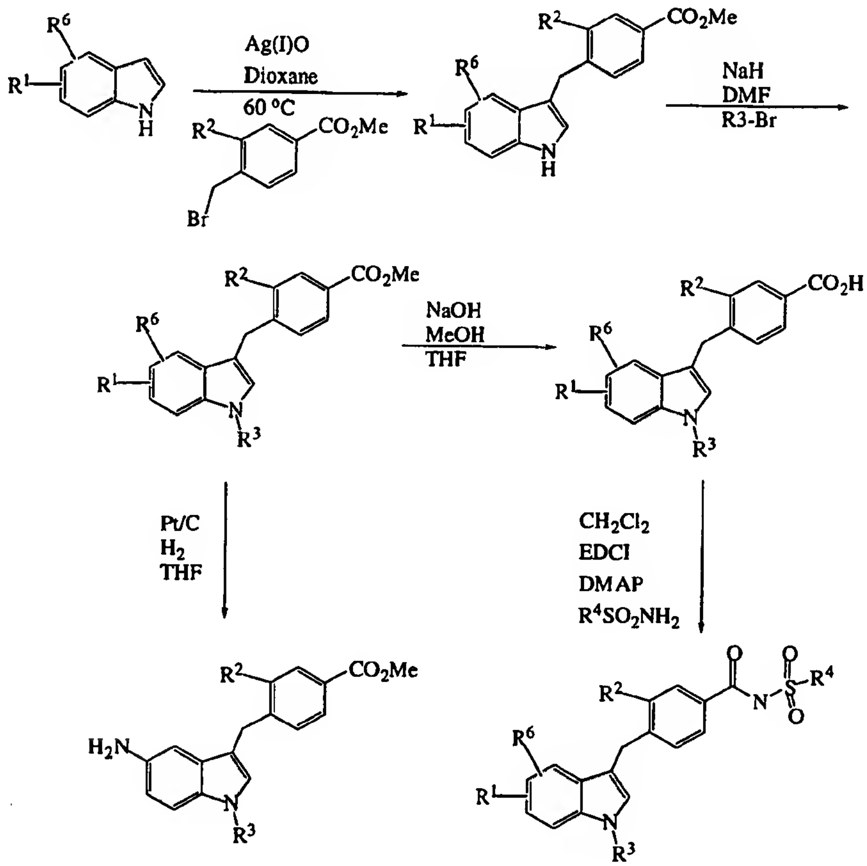
Compounds of the present invention invention can be made according to the methods and examples described below. Synthesis of preferred compounds of the present invention are described in the examples below.

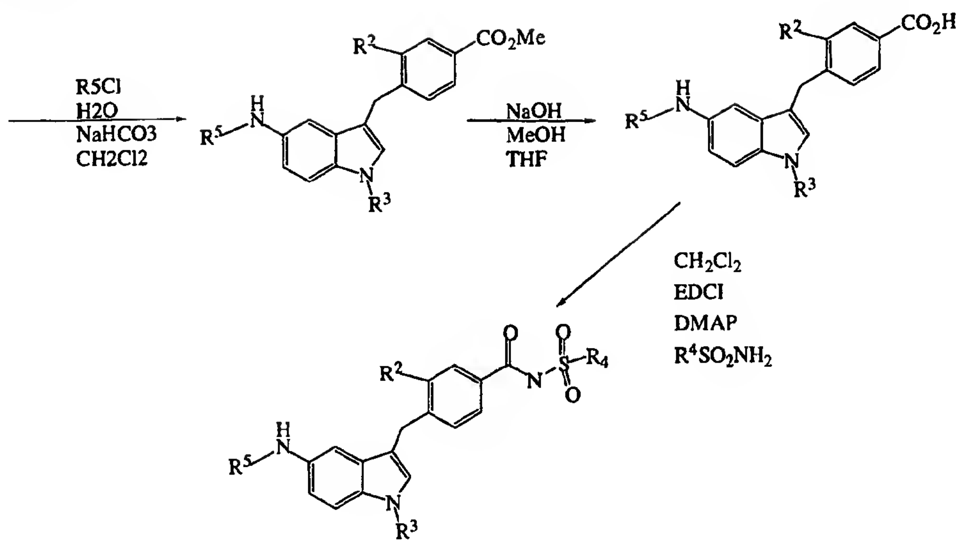
Method A

The indole may be alkylated at the c-3 position with the appropriate alkyl bromide and treatment with a lewis acid such as silver(I)oxide or silver tetrafluoroborate in a solvent such as dioxane or THF at elevated temperatures of 50 °C - 100 °C. Alternatively it may be alkylated in a two step procedure by treatment of the indole with n-BuLi in a solvent such as THF or ether followed by ZnCl2 and then concentrated and treated with the appropriate alkylating agent in a variety of solvents such as THF, ether, toluene or benzene. The indole nitrogen may then be alkylated by treatment with a strong base such as sodium bis(trimethylsilyl)amide, n-BuLi, sodium hydride or potassium hydride in a solvent such as DMF, DMSO or THF followed by exposure to the appropriate alkyl halide. The ester can be hydrolyzed under basic conditions with sodium hydroxide in water and methanol and THF. Alternatively it may be cleaved by treatment with sodium thiomethoxide in a solvent such as THF or DMF at elevated temperatures (50 °C - 100 °C). The product acid by be coupled to a sulfonamide by the agency of a variety of coupling reagents such as DCC, EDCI or carbonyl diimidazole in a solvent such as THF, methylene chloride, dichloroethane or DMF in the presence of a base such as triethyl amine and/or N, N-dimethyl pyridine. In the case of R1 = nitro the nitro group can be reduced by exposure to Pt/C in the presence of hydrogen in a solvent such as methanol, ethyl acetate or THF. The resulting amine can be acylated or sulfonylated by exposure to the appropriate agent in the presence of a base such as triethyl amine, sodium bicarbonate or pyridine in a biphasic solvent system such as methylene chloride:water (1:1) or THF:water (1:1) or a monophasic organic solvent such as methylene chloride, THF or DMF with triethylamine. The resulting

acid may then be hydrolyzed and modified as described above. Also in the case R1 = Br, it may be replaced with the copper salt of the desired nucleophile such as thiomethoxide, methoxide or sulphinic acid.

Method A



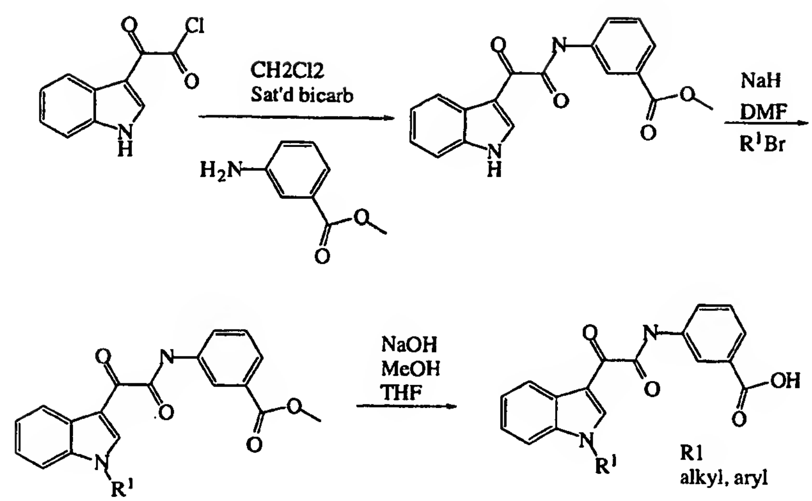


R^1	R^2	R^3	R^4	R^5	R^6
NH_2, nitro, halogen alkyl 5,6-methylenedioxy methoxy	H, MeO	alkyl, alkenyl, aryl	alkyl, aryl heterocyclic	aryl carbamate alkyl urea alkyl amide aryl amide sulfonamide	H, halogen, methoxy

Method B

The indoleglyoxalyl chloride may be reacted with the desired amino ester in a biphasic system with methylene chloride and saturated sodium bicarbonate or in a monophasic system with a solvent such as methylene chloride, ethyl acetate or THF and a base such as triethylamine, Hunigs base or pyridine. The indole nitrogen may then be alkylated with a variety of alkylating reagents in a solvent such as DMF, DMSO or THF and a base such as sodium hydride, n-BuLi or potassium bis(trimethylsilyl)amide. The ester may then be hydrolyzed with sodium hydroxide or lithium hydroxide in a solvent system such as water:methanol:THF.

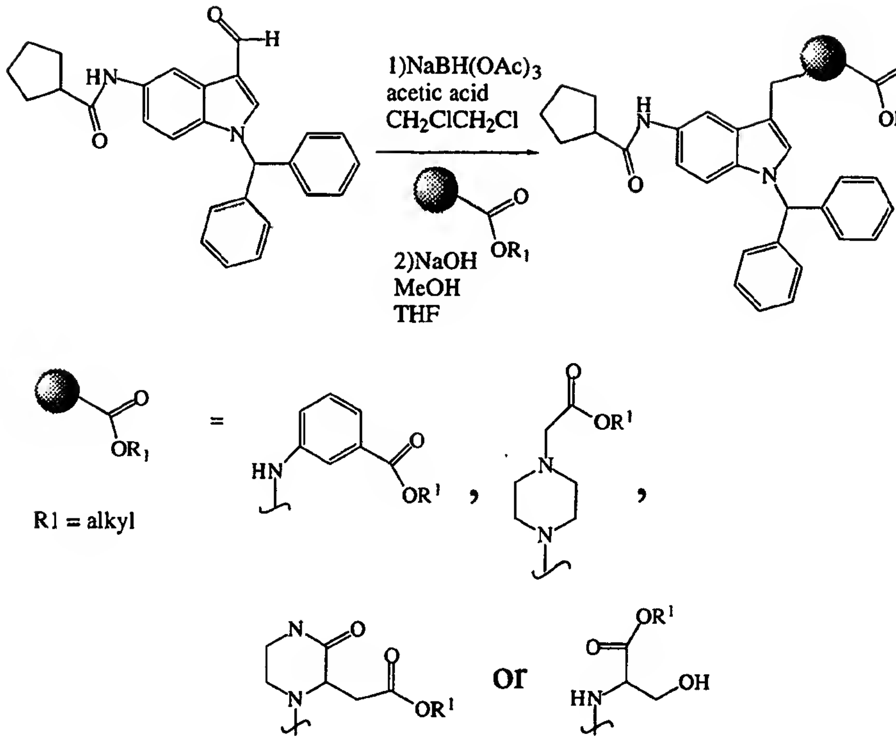
Method B



Method C

The 3-carboxyindole is elaborated via reductive amination by allowing the aldehyde to condense with an amino ester in a solvent such as methylene chloride or dichloromethane with or without acetic acid. The resulting imine is reduced in-situ with a reducing agent such as sodium borohydride, sodium cyanoborohydride or sodium triacetoxyborohydride. The acid is then prepared by hydrolysis of the resulting ester with sodium hydroxide or lithium hydroxide in a solvent system such as water:methanol:THF.

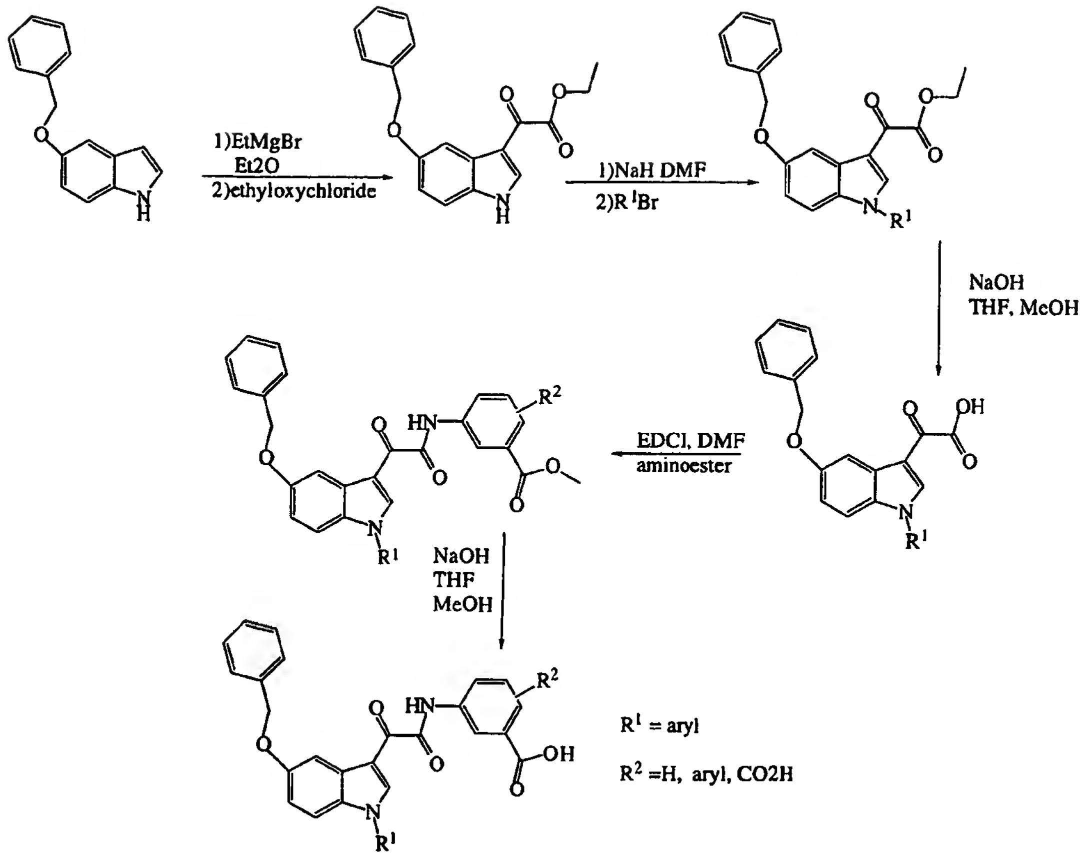
Method C



Method D

5-benzyloxyindole may be treated with a base such at methyl or ethyl grignard and acylated at the 3-position with ethyloxychloride in a suitable solvent such at ether or THF. The indole nitrogen may then be alkylated with a benzylbromide by the action of a base such as sodium hydride or n-butyllithium in a solvent such a THF or DMF. The ester is then hydrolysed under basic conditions with sodium hydroxide or tetrabutylammonium hydroxide in a suitable solvent system such at water:MeOH:THF. Coupling of the appropriate aminoester may then be effected by the use of a coupling agent such as DCC or EDCI in a solvent such as methylenechloride, THF or DMF. The target acid may the be revealed by hydrolysis of the ester under the same conditions discussed above.

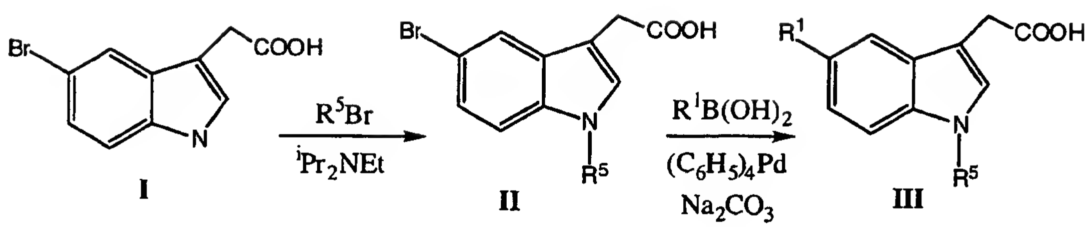
Method D

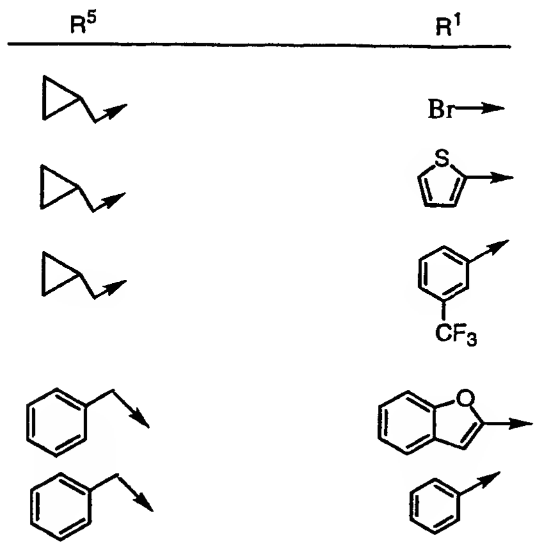


Method E

Indole-3-acetic acid was alkylated with an appropriate alkyl bromide which was then subjected to Suzuki coupling conditions using Pd(PPh3)4 as a catalyst in a mixed solvent (ethanol-benzene-water) at elevated temperature to give the 1-alkyl-5-substituted indole.

Method E

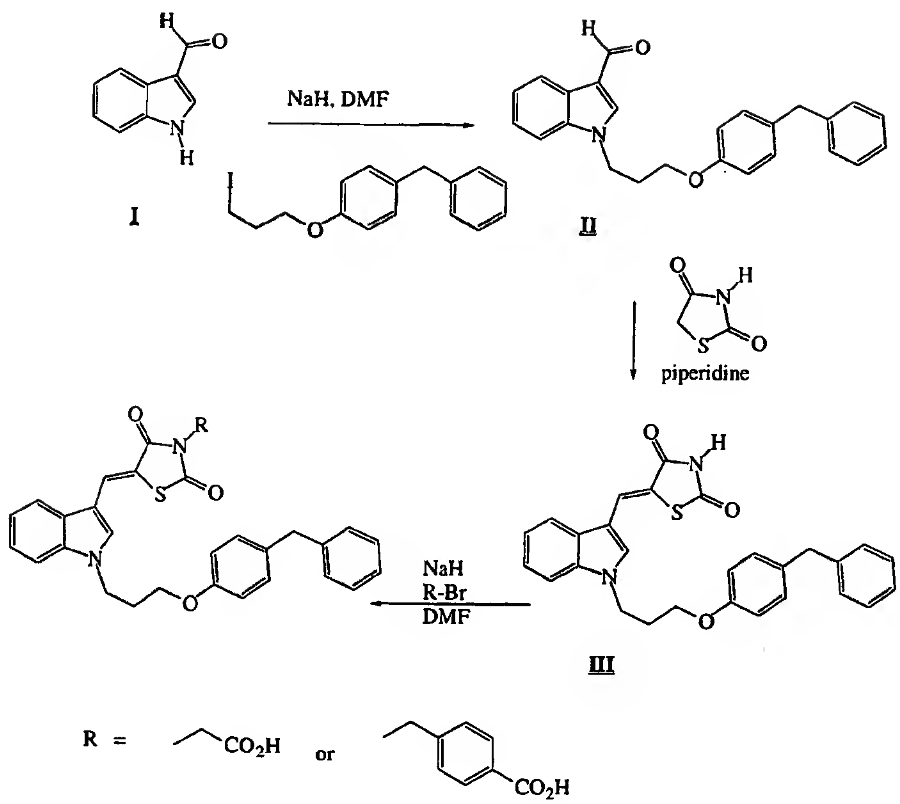




Method F

Alkylation of the nitrogen atom of I with a suitable base such a sodium hydride or potassium carbonate and an alkyl halide gave the aldehyde II. The aldehyde could be transformed to the thiazolidinedione III using a base such as piperdine and isolated with an acid such as acetic acid. Deprotonation with a suitable base such as sodium hydride and alkylation on the nitrogen atom of the thiazolidinedione with selected electrophiles such as alkyl or benzyl halides provided compounds such as IV.

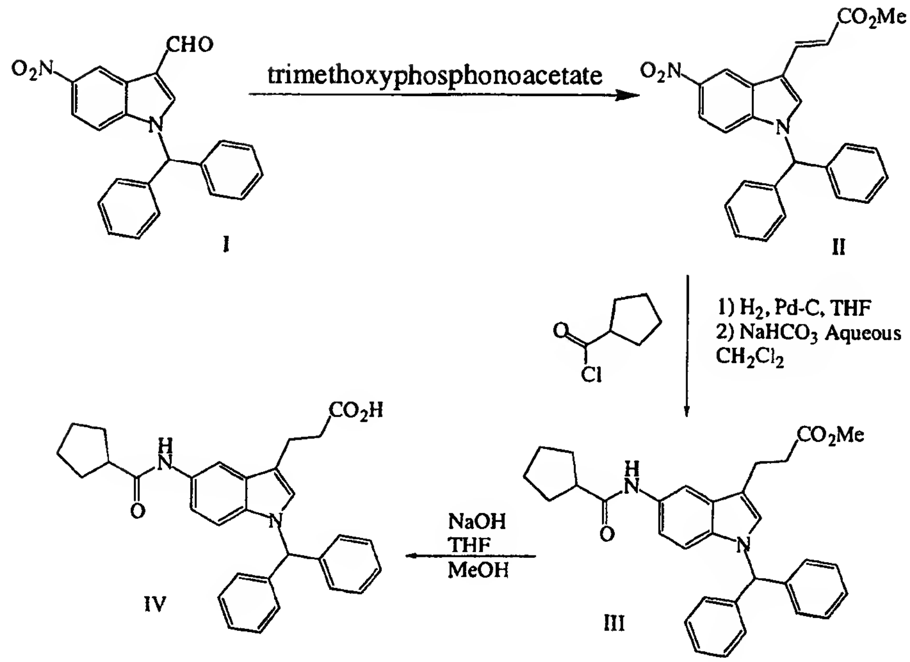
Method F



Method G

The nitro-indole I was converted to the unsaturated ester via a Horner-Wittig reaction with trimethoxyphosphonoacetate in a suitable solvent such as tetrahydrofuran. Reduction of the nitro group of II can be accomplished via hydrogenation with palladium on carbon in the presence of hydrogen and acylation of the resulting amine under Schotten-Bowmann conditions to give amides such as III. Saponification of the ester function gave the acid-indole IV.

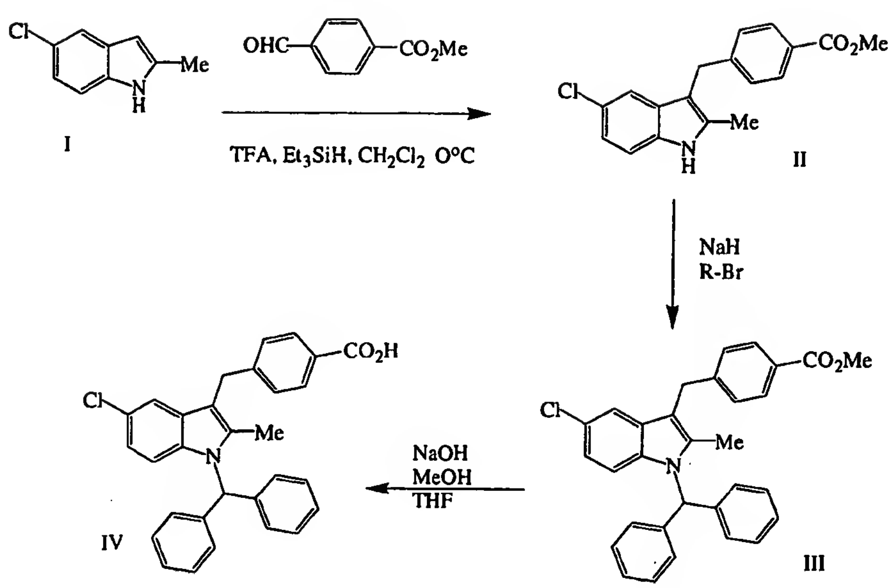
Method G



Method H

5-Chloro-2-methylindole could be reductively alkylated at the 3-position with a suitable aldehyde in the presence of an acid such as trifluoroacetic acid and a reducing agent such as triethylsilane in a suitable solvent such as methylene chloride to give the ester II. The nitrogen atom could be alkylated by treatment with a suitable base such as sodium hydride and diphenyl bromo methane and the resulting compound III could be saponified to give IV.

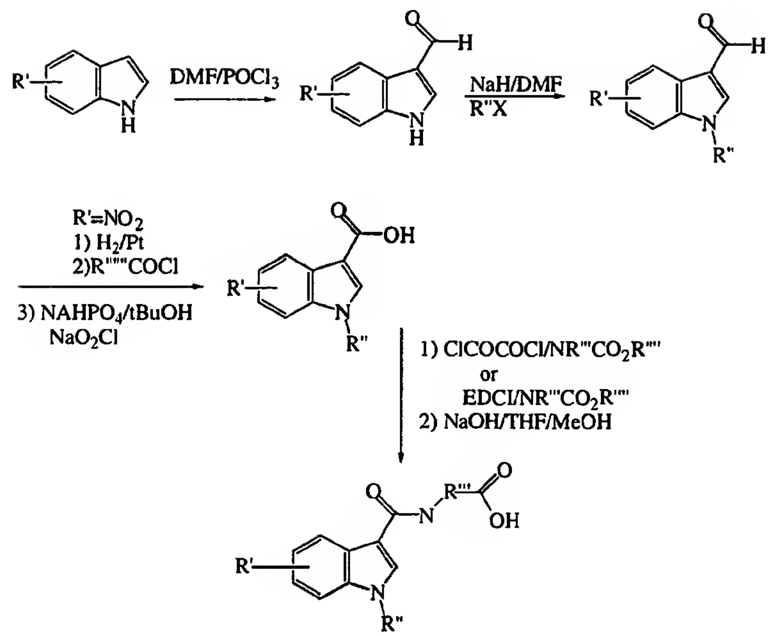
Method H



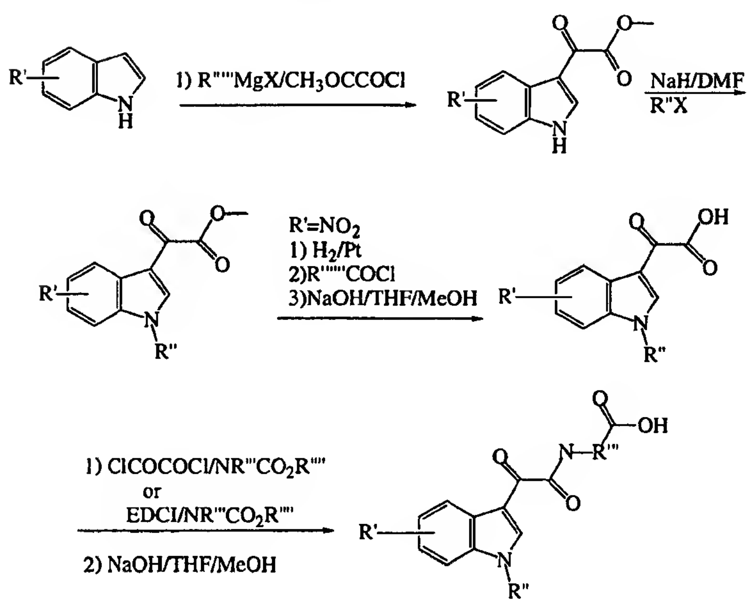
Method I

The starting indole is C3 functionalized by either reaction of DMF/POCl3 or by reacting the magnesium salt of the indole with methyl oxalyl chloride. The resulting esters and aldehydes were then Nalkylated by treating the salt of the indole, generated by treating the indole with a strong base, with a variety of alkyl halides. In th case of the aldehydes, when r' is a nitro group, the nitro is reduced to the amine using Pt/C and H2 or copper acetate/sodium borohydride and then acylated usind various acid chlorides, isocyanates, chloroformates or reductively alkylated using aldehydes and sodium triacetoxyborohydride. These aldehydes could then be oxidised to the desired acid which could be coupled to an amino alkyl or aryl esters by an EDCI coupling method or by first transforming the acid into the acid chloride under the action of oxalyl chloride and the reacting this with an amino alkyl or aryl ester. These were then hydrolyzed to yield the final product. The esters generated above could be treated in a similar fashion. The ester could hydrolyzed and then coupled to an amino alkyl or aryl esters by an EDCI coupling method or by first transforming the acid into the acid chloride under the action of oxalyl chloride and the reacting this with an amino alkyl or aryl ester. These were then hydrolyzed to yield the final product.

Method I(a)



Method I(b)

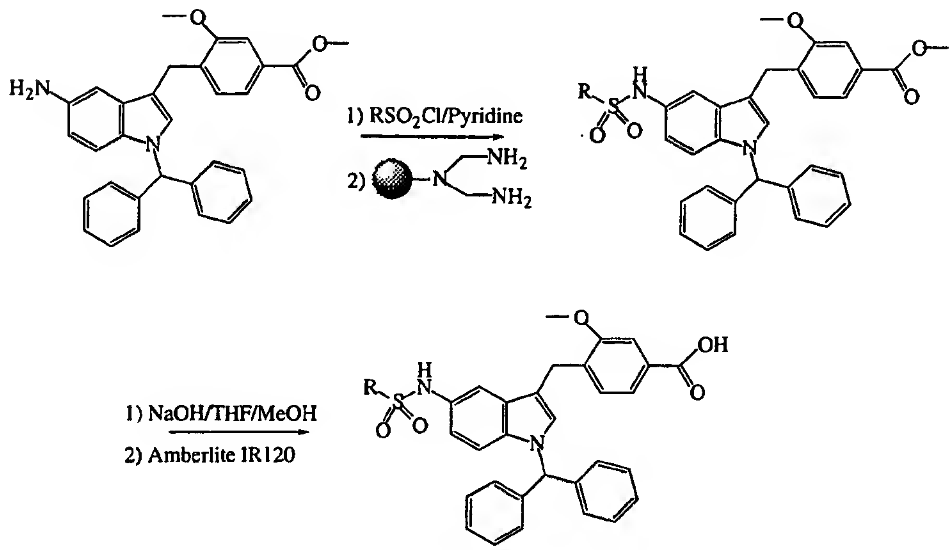


Method J

The starting amine was treated with various sulfonyl chlorides in the presence of pyridiine and then the excess sulfonylchloride was scavenged by adding a polymer bound amine. The

desired products where then hydrolyzed using sodium hydroxide in THF/MeOH and the reaction was aidified using IR-120 resin to yield the desired products.

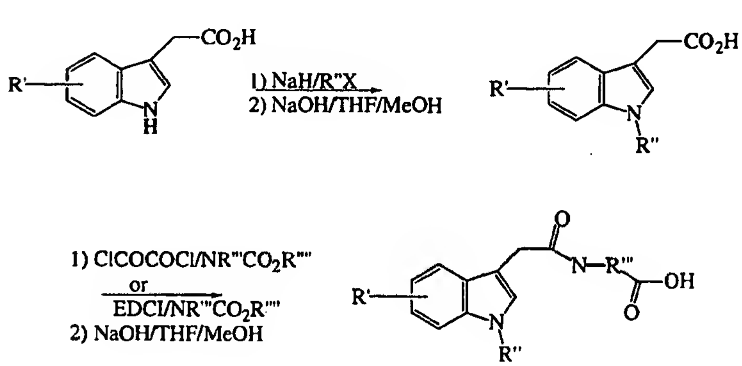
Method J



Method K

The starting indole was bis alkylated by the addition of a strong base such as sodium hydride and then an alkylating agent such as an alkyl or aryl halide followed by the hydrolysis of the resulting ester with sodium hydroxide in THF/MeOH. The acid was then coupled with an alkyl or aryl amino ester and then hydrolyzed to yield the desired acid.

Method K



Example 1

4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1 - To a solution of 5-nitro indole (21.24 g, 131 mmol) in dioxane (128 mL) in a reaction vessel wrapped in aluminum foil is added silver(I)oxide (30.34 g, 131 mmoL, 1.5 eq) and methyl 4-(bromomethyl)-3-methoxy-benzoate (34 g, 131 mmol) and the mixture is brought to 60 °C and stirred 20 h. The reaction is cooled, filtered through celite, taken up in ethyl acetate (500 mL), washed with brine (2 X 50 mL), dried ($MgSO_4$) and filtered. The crude material was purified by silica chromatography (15% ethyl acetate / hexanes) to afford the desired product (5.8 g, 55%).

Step 2 - The C3-alkylated indole (1.5 g, 4.4 mmol) was dissolved with 15 mL THF. In a separate flask, NaH (185 g, 4.61 mmol) was suspended with 25 mL THF at 0 °C. The solution of starting material was cannulated into the NaH suspension, giving a deep red solution. This was then allowed to stir at room temperature for 10 minutes. 1-iodopropane was added (0.47 mL, 1.1 mmol) and the reaction was allowed to pr°ceed overnight at room temperature. As the reaction was not complete (TLC) and additional 0.5 mL of 1-iodopropane was added and the reaction continued for another 3 h. There was no change in the TLC and the reaction was poured into cold 1 N HCl and extracted with CH_2Cl_2 (3 X 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated to yield the crude N-alkylated nitroindole. The crude material was absorbed onto silica and loaded onto a silica gel column. The column was eluted with 100% CH_2Cl_2 to give the pure yellow N-alkylated nitroindole (0.96 g, 57%).

Step 3 - The N-alkylated nitroindole (0.95 g) was dissolved with 40 mL anhydrous THF. The system was purged with argon. To the clear, yellow solution, Pt/C (0.462 g) was added. The argon was then removed by evacuation and hydrogen was introduced to the system. The reaction was stirred 6.5 h. The hydrogen was evacuated and argon was then purged through the system. The reaction mixture was filtered through celite with THF. The solvent was removed by rotary evaporation to give the crude amine as a dark oil. Chromatography (5% ethyl acetate/CH_2Cl_2) afforded the desired product (0.7 g, 80%)

Step 4 - The amine from above (0.7 g) was dissolved in 40 mL CH_2Cl_2. 4-methylmorpholine (0.3 mL, 3.0 mmol) and cyclopentyl chloroformate (383 mg, 2.57 mmol) were then added to give a yellow/orange solution. The reaction was allowed to proceed at room temperature for 3 h. The reaction mixture was acidified with 1 N HCl and the mixture was extracted with 50 mL CH_2Cl_2. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated to give the crude carbamate. The crude product was absorbed onto silica gel and loaded onto a silica gel column. The column was eluted with 100% CH_2Cl_2 to afford the desired product (0.87 g, 39%) as a yellow foam.

Step 5 - The carbamate (0.831 g) was dissolved with hydrolysis solution (2:1:1 THF:MeOH:2N NaOH) and the reaction was allowed to proceed for 5.25 h. The reaction was acidified to pH 2 with 2N HCl and extracted with CH_2Cl_2. The organic layer was washed with water and brine. The combined organic layers were then dried over $MgSO_4$, filtered and evaporated to yield the crude acid, which was recrystallized from CH_2Cl_2 to afford the title compound (0.575 g, 71%) as pink crystals.
MS: m/z (M-1) 449

Example 2

Cyclopentyl N-{3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1-propyl-1H-indol-5-yl}carbamate

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate.

Example 3

4-[(1-benzhydryl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate.

Example 4

4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(2-naphthylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate.

MS: m/z (M-1) 547

Example 5

4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(cyclopropylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate.

MS: m/z (M-1) 461

Example 6

4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(4-pyridinylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate.

Example 7

4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-isopropyl-1H-indol-3yl)methyl]-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2 - The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3 - The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4 - The title compound is prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 449

Example 8

4-[(1-cyclopentyl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1 - The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent.

Step 2

The intermediate 5-amino indole is prepared as in Example 1, step 3, using the above intermediate.

Step 3

The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 4

The title compound is prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 475

Example 9

4-[(1-benzhydryl-5-{[(butylamino)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent and the intermediate 5-amino indole is prepared as in Example 1, step 3, using the 5-nitro indole intermediate. The intermediate urea is prepared as in Example 1, step 4, using the appropriate acylating agent. The title compound is prepared as in Example 1, step 5, using the urea intermediate.

MS: m/z (M-1) 560

Example 10

4-({1-benzhydryl-5-[(methylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent followed by preparation of the intermediate 5-amino indole as in Example 1, step 3, using the 5-nitro indole. The intermediate sulfonamide is next prepared as in Example 1, step 4, using the appropriate acylating agent. The title compound is then prepared as in Example 1, step 5, using the sulfonamide intermediate. MS: m/z (M-1) 539

Example 11

4-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent and intermediate 5-amino indole is prepared as in Example 1, step 3, using this 5-nitro indole intermediate. The corresponding intermediate amide is then prepared as in Example 1, step 4, using the appropriate acylating agent. The final title compound is prepared as in Example 1, step 5, using this amide intermediate. MS: m/z (M-1) 557

Example 12

4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

The intermediate 5-nitro indole is prepared as in Example 1, step 2, using the appropriate alkylating agent and the title compound is prepared as in Example 1, step 5, using this intermediate. MS: m/z (M-1) 657

Exmaple 13

4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

The intermediate 5-bromo indole is prepared as in Example 1, step 1, using the appropriate indole and as in Example 1, step 2, using the appropriate alkylating agent. The title compound is then prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 526

Example 14

4-[(1-benzhydryl-5-fluoro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

The intermediate 5-fluoro indole is prepared as in Example 1, step 1, using the appropriate indole and as in Example 1, step 2, using the appropriate alkylating agent. The title compound is prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 464

Example 15

4-[(1-benzhydryl-5-methyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

The intermediate 5-methyl indole is prepared as in Example 1, step 1, using the appropriate indole and as in Example 1, step 2, using the appropriate alkylating agent. The title compound is then prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 460

Example 16

4-[(5-benzhydryl-5H-[1,3]dioxolo[4,5-f]indol-7-yl)methyl]-3-methoxybenzoic acid

The intermediate 5,6-methylenedioxy indole is prepared as in Example 1, step 1, using the appropriate indole and as in Example 1, step 2, using the appropriate alkylating agent. The title compound is then prepared as in Example 1, step 5, using the above intermediate. MS: m/z (M-1) 490

Example 17

4-[(1-benzhydryl-5-cyano-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1

To the intermediate from Example 13, step 2 (0.25 g, 0.46 mmol), in DMF (1 mL) is added CuCN (0.05g, 1.2 eq) and the reaction mixture is stirred at 145 °C overnight and then cooled. To the cooled reaction mixture is added $FeCl_3$ (0.09 g, 1.2 eq). The reaction mixture is stirred 5 min, taken up in ethyl acetate (30 mL), washed with brine (3 X 10 mL), dried ($MgSO_4$), filtered and concentrated. The product was purified by silica chromatography (20% ethyl acetate/hexanes) to afford the intermediate ester (0.2 g, 89%) as a colorless oil.

Step 2

To the intermediate ester (0.2 0.41 mmol) in DMF (2 mL) is added sodium thiomethoxide (0.1 g, 3.4 eq) and the reaction mixture is stirred at 90 °C for 10 min. The reaction is cooled, poured into ethyl acetate (5 mL), washed with sodium biphosphate (1 X 2 mL), brine (2 X 2 mL), dried ($MgSO_4$), filtered and concentrated. Purification by silica chromatography (1% acetic acid, 25% ethyl acetate/hexanes) afforded the title compound (0.114 g, 59%) as a colorless amorphous powder. MS: m/z (M-1) 471

Example 18

4-{[1-benzhydryl-5-(methylsulfonyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1

To the intermediate from Example 13, step 3 (1 g, 1.9 mmol), in a solution of THF (2 mL) and methanol (2 mL) is added sodium hydroxide (0.41 mL, 4.63 M, 1 eq). The mixture is stirred for 20 min and then concentrated. The residual water is chased off by the addition of toluene and it's removal (3 X) a white powder (1 g, 100%).

Step 2

To the sodium salt prepared above (0.88 g, 1.6 mmol) in DMF (3 mL) is added methanesulfinic acid, sodium salt (0.72 g, 4.4 eq) and CuI (0.74 g, 2.4 eq). The reaction mixture is stirred at 130 °C overnight, cooled, taken up in ethyl acetate (50 mL) and acetic acid

(10 mL), filtered (celite), washed with brine (4 X 10 mL), dried ($MgSO_4$), filtered and concentrated. Silica chromatography (1% acetic acid, 25% ethyl acetate/hexanes - 1% acetic acid, 50% ethyl acetate/hexanes) afforded the title compound (0.2 g, 24%) as a colorless amorphous solid. MS: m/z (M-1) 524

Example 19

Cyclopentyl N-{1-benzhydryl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

To the product of Example 3, step 4 (0.5 g, 0.87 mmol), in CH_2Cl_2 (4 mL) is added EDCI (0.2 g, 1.0 mmol, 1.2 eq), DMAP (0.011 g, 0.087 mmol, 0.1 eq) and ortho-toluene sulfonamide. The reaction is stirred overnight at room temperature, taken up in ethyl acetate (50 mL), washed with sodium biphosphate (1 X 10 mL), brine (2 X 10 mL), dried ($MgSO_4$), filtered and concentrated. Silica chromatography (1% acetic acid, 25% ethyl acetate/hexanes) afforded the title compound (0.4 g, 63%) as a colorless solid.

Example 20

Cyclopentyl N-{3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1-propyl-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 1, step 5, and the appropriate sulfonamide.

Example 21

Cyclopentyl N-{1-(cyclopropylmethyl)-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 5, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 614

Example 22

Cyclopentyl N-[3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1-(4-pyridinylmethyl)-1H-indol-5-yl]carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 6, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 651

Example 23

Cyclopentyl N-[3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1-(2-naphthylmethyl)-1H-indol-5-yl]carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 4, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 700

Example 24

Cyclopentyl N-{1-isopropyl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 7, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 602

Example 25

Cyclopentyl N-{1-cyclopentyl-3-[2-methoxy-4-({[(2-methylphenyl) sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 8, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 628

Example 26

Cyclopentyl N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 704

Example 27

cyclopentyl N-[1-benzhydryl-3-(2-methoxy-4-{[(methylsulfonyl)amino]carbonyl}benzyl)-1H-indol-5-yl]carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 650

Example 28

cyclopentyl N-{1-benzhydryl-3-[4-({[(2-chlorophenyl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide.

Example 29

cyclopentyl N-(3-{4-[({[5-(acetylimino)-4-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1-benzhydryl-1H-indol-5-yl)carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide.

Example 30

cyclopentyl N-(1-benzhydryl-3-{4-[({[5-(dimethylamino)-1-naphthyl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1H-indol-5-yl)carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide.

Example 31

cyclopentyl N-[1-benzhydryl-3-(4-{[(benzylsulfonyl)amino]carbonyl}-2-methoxybenzyl)-1H-indol-5-yl]carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 726

Example 32

cyclopentyl N-{1-benzhydryl-3-[4-({[(2,4-dimethyl-1,3-thiazol-5-yl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 747

Example 33

cyclopentyl N-{1-benzhydryl-3-[4-({[(3,5-dimethyl-4-isoxazolyl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide. MS: m/z (M-1) 731

Example 34

cyclopentyl N-(3-{4-[({[5-(acetylamino)-1,3,4-thiadiazol-2-yl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1-benzhydryl-1H-indol-5-yl)carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide.

Example 35

cyclopentyl N-(1-benzhydryl-3-{2-methoxy-4-[({[4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)phenyl]sulfonyl}amino)carbonyl]benzyl}-1H-indol-5-yl)carbamate

The title compound is prepared as illustrated in Example 19 starting with the product of Example 3, step 4, and the appropriate sulfonamide.

Example 36

N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoyl}-2-methylbenzenesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 12, step 2, and the appropriate sulfonamide. MS: m/z (M-1) 644

Example 37

N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro)methanesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 12, step 2, and the appropriate sulfonamide. MS: m/z (M-1) 622

Example 38

N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]-3-methoxybenzoyl}-2-methylbenzenesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 13, step 2, and the appropriate sulfonamide. MS: m/z (M-1) 679

Example 39

N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro)methanesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 13, step 2, and the appropriate sulfonamide.

MS: m/z (M-1) 657

Example 40

N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino} carbonyl)benzyl]-1H-indol-5-yl}cyclopentanecarboxamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 11, step 4, and the appropriate sulfonamide.

MS: m/z (M-1) 688

Example 41

N-[4-({1-benzhydryl-5-[(methylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoyl](trifluoro)methanesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 10, step 4, and the appropriate sulfonamide.

MS: m/z (M-1) 670

Example 42

N-{4-[(1-benzhydryl-5-{[(butylamino)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro)methanesulfonamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 9, step 4, and the appropriate sulfonamide.

MS: m/z (M-1) 691

Example 43

N-{1-benzhydryl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino} carbonyl)benzyl]-1H-indol-5-yl}cyclopentanecarboxamide

The title compound is prepared as illustrated in Example 19 starting with the product of Example 11, step 4, and the appropriate sulfonamide.

MS: m/z (M-1) 710

Example 44

4-({5-[(cyclopentylcarbonyl)amino]-1-[phenyl(2-pyridinyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1

The intermediate 5-amino indole is prepared as in Example 1, step 3.

Step 2

The intermediate sulfonamide is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 3

The intermediate acid is prepared as in Example 1, step 5, using the above intermediate.

Step 4

The title compound is prepared as illustrated in Example 19 starting with the intermediate above and the appropriate sulfonamide.

MS: m/z (M-1) 738

Example 45

N-[4-({1-benzhydryl-5-[(benzylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoyl](trifluoro)methanesulfonamide

Step 1

The intermediate 5-amino indole is prepared as in Example 1, step 3.

Step 2

The intermediate sulfonamide is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 3

The intermediate acid is prepared as in Example 1, step 5, using the above intermediate.

Step 4

The title compound is prepared as illustrated in Example 19 starting with the intermediate above and the appropriate sulfonamide.

MS: m/z (M-1) 746

Example 46

N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino} carbonyl)benzyl]-1H-indol-5-yl}-3-thiophenecarboxamide

Step 1

The intermediate 5-amino indole is prepared as in Example 1, step 3.

Step 2

The intermediate amide is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 3

The intermediate acid is prepared as in Example 1, step 5, using the above intermediate.

Step 4

The title compound is prepared as illustrated in Example 19 starting with the intermediate above and the appropriate sulfonamide.

MS: m/z (M-1) 702

Example 49

benzyl N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

Step 1

The intermediate 5-amino indole is prepared as in Example 1, step 3.

Step 2

The intermediate carbamate is prepared as in Example 1, step 4, using the appropriate acylating agent.

Step 3

The intermediate acid is prepared as in Example 1, step 5, using the above intermediate.

Step 4

The title compound is prepared as illustrated in Example 19 starting with the intermediate above and the appropriate sulfonamide.

MS: m/z (M-1) 726

Example 50

4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoic acid

Step 1

The intermediate 3-alkylated 5-nitroindole is prepared as illustrated in Example 1, step 1, using the appropriate alkylating agent.

Step 2

The intermediate 3-alkylated 5-nitroindole is N-alkylated as illustrated in Example 3, step 1.

Step 3

The title compound is prepared as illustrated in Example 1, step 5.

MS: m/z (M-1) 461

Example 51

4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoic acid

Step 1

The intermediate 3-alkylated 5-bromoindole is prepared as illustrated in Example 13, step 1, using the appropriate alkylating agent.

Step 2

The intermediate 3-alkylated 5-nitroindole is N-alkylated as illustrated in Example 13, step 2.

Step 3

The title compound is prepared as illustrated in Example 13, step 3.

MS: m/z (M-1) 494

Example 52

4-[(1-benzhydryl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]benzoic acid

Step 1

Starting with the material prepared in Example 50, step 2, the desired intermediate is prepared as illustrated in Example 3, step 2.

Step 2

The intermediate carbamate is prepared from the above intermediate as illustrated in Example 3, step 3.

Step 3

The title compound is prepared from the above intermediate as illustrated in Example 3, step 4.

MS: m/z (M-1) 543

Example 53

cyclopentyl N-{1-benzhydryl-3-[4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared from the product of Example 52, step 3, as illustrated in Example 19. MS: m/z (M-1) 697

Example 54

cyclopentyl N-{1-benzhydryl-3-[4-({[(trifluoromethyl)sulfonyl]amino} carbonyl)benzyl]-1H-indol-5-yl}carbamate

The title compound is prepared from the product of Example 52, step 3, as illustrated in Example 26. MS: m/z (M-1) 674

Example 55

N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoyl} (trifluoro)methanesulfonamide

The title compound is prepared from the product of Example 55, step 3, as illustrated in Example 26. MS: m/z (M-1) 592

Example 56

N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoyl}-2-methylbenzenesulfonamide

The title compound is prepared from the product of Example 55, step 3, as illustrated in Example 19. MS: m/z (M-1) 614

Example 57

N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoyl}-2-methylbenzenesulfonamide

The title compound is prepared from the product of Example 51, step 3, as illustrated in Example 38. MS: m/z (M-1) 649

Example 58

N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoyl} (trifluoro)methanesulfonamide

The title compound is prepared from the product of Example 51 step 3 as illustrated in Example 39. MS: m/z (M-1) 627

Example 59

3-({2-[1-(4-benzylbenzyl)-1H-indol-3-yl]-2-oxoacetyl}amino)benzoic acid

Step 1 - To a solution of methyl 3-aminobenzoate (2.4 g, 16.0 mmol) in CH_2Cl_2 (50 mL) and saturated sodium bicarbonate (50 mL) at 5 °C is added 3-indolylglyoxalyl chloride (3.0 g, 14.4 mmol). The reaction is stirred to room temperature over 2 h, taken up in ethyl acetate (200 mL), washed with brine (3 X 50 mL), dried ($MgSO_4$), filtered and concentrated.

Crystallization of the crude material afforded the desired intermediate (2.7 g, 58%) as a colorless solid.

Step 2 - To a solution of the above intermediate (0.3 g, 0.93 mmol) in DMF (1.5 mL) at 0 °C is added potassium bis(trimethylsilyl)amide (0.41 g, 2.06 mmol). After the reaction is stirred at room temperature 30 min 4-benzylbenzyl bromide (0.27 g, 1.03 mmol) is added. The reaction is stirred 3 h, taken up in ethyl acetate (10 mL), washed with brine (3 X 2 mL), dried ($MgSO_4$), filtered and concentrated. Radial silica chromatography (2 mm, 10% - 35% ethyl acetate/hexanes) afforded the desired intermediate (0.19 g, 41%) as a colorless oil.

Step 3 - The ester obtained in step 2 was treated with sodium hydroxide (2 mL, 5 M) in THF (5 mL) and MeOH (2 mL). The reaction was stirred overnight, taken up in ethyl acetate (50 mL), washed with sodium biphosphate (1 X 10 mL), brine (2 X 10 mL), dried ($MgSO_4$), filtered and concentrated. Trituration of the material in ethyl acetate with hexanes afforded the title compound (0.105 g, 60%) as a colorless solid. MS: m/z (M-1) 487

__Example 60__

__3-({2-[1-(4-{[3,5-bis(trifluoromethyl)phenoxy]methyl}benzyl)-1H-indol-3-yl]-2-oxoacetyl}amino)benzoic acid__

The intermediate prepared in Example 59, step 1, was N-1 alkylated with the appropriate reagent using the procedure described in Example 59, step 2.

Step 2

The product ester was hydrolyzed as described in Example 59, step 3.

MS: m/z (M-1) 639

__Example 61__

__3-{[2-(1-benzhydryl-1H-indol-3-yl)-2-oxoacetyl]amino}benzoic acid__

The intermediate prepared in Example 59, step 1, was N-1 alkylated with the appropriate reagent using the procedure described in Example 59, step 2.

Step 2

The product ester was hydrolyzed as described in Example 59, step 3.

MS: m/z (M-1) 473

Example 62

3-[(2-{1-[3-(4-benzylphenoxy)propyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1

The intermediate prepared in Example 59, step 1, was N-1 alkylated with the appropriate reagent using the procedure described in Example 59, step 2.

Step 2

The product ester was hydrolyzed as described in Example 59, step 3.

MS: m/z (M-1) 531

Example 63

3-[(2-{1-[3,4-bis(benzyloxy)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1

The intermediate prepared in Example 59, step 1, was N-1 alkylated with the appropriate reagent using the procedure described in Example 59, step 2.

Step 2

The product ester was hydrolyzed as described in Example 59, step 3.

MS: m/z (M-1) 609

Example 64

3-[(2-{1-[2-(benzylsulfonyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1

The intermediate prepared in Example 59, step 1, was N-1 alkylated with the appropriate reagent using the procedure described in Example 59, step 2.

Step 2

The product ester was hydrolyzed as described in Example 59, step 3.

MS: m/z (M-1) 551

Example 65

3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)amino]benzoic acid

Step 1

To a solution of the aldehyde prepared in Example 114, step 3 (0.3 g, 0.7 mmol) in dichloroethane (2 mL) and DMF (1 mL) is added methyl 3-amino benzoate (0.113 g, 0.735

mmol, 1.05 eq) and acetic acid (0.13 mL, 2.1 mmol, 3 eq). After stirring 30 min sodium triacetoxyborohydride (0.18 g, 0.84 mmol, 1.2 eq) is added and the reaction is allowed to stir an additional 4 h after which it is taken up in ethyl acetate (20 mL), washed with saturated sodium bicarbonate (1 X 10 mL), brine (2 X 5 mL), dried ($MgSO_4$), filtered and concentrated. Silica chromatography (30% ethyl acetate/hexanes) afforded the desired intermediate (0.24 g, 60%) as a colorless oil.

Step 2

The product ester was hydrolyzed as described in Example 59 step 3 to give the title compound (0.11 g, 55%). MS: m/z (M-1) 542

Example 66

2-[4-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)piperazino]acetic acid

The title compound was prepared as described in Example 65 using the appropriate amine. MS: m/z (M-1) 549

Example 67

2-[1-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)-3-oxo-2-piperazinyl]acetic acid

The title compound was prepared as described in Example 65 using the appropriate amine. MS: m/z (M-1) 563

Example 68

2-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)amino]-3-hydroxypropanoic acid

The title compound was prepared as described in Example 65 using the appropriate amine. MS: m/z (M-1) 510

Example 69

2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetic acid

Step 1 - Ethylmagnesium bromide (3M in ether, 57 mL) was diluted in ether (50 mL). 5-Benzyloxyindole (12.7 g) dissolved in ether (150 mL) was added to the Grignard solution at - 78 °C. After 1.25 h, ethyloxalyl chloride (17.12 g) was added. The reaction was stirred 15 min, quenched with saturated sodium bicarbonate, taken up in ethyl acetate and washed with water, dried ($MgSO_4$), filtered and concentrated. The resulting solid was triturated with ethanol

and stirred for 1 h. The desired product (5.75 g, 31%) was isolated as a yellow solid and used without further purification.

Step 2 - To the above indole in DMF at 0 °C was added sodium hydride (0.4 g, 60% dispersion in oil). After warming to room temperature, 4-benzylbenzylbromide (2.2 g) was added and the mixture was stirred overnight. As the reaction was not yet done (TLC) additional 4-benzylbenzylbromide (1.0 g) was added and the reaction stirred for 2.5 h. The reaction was taken up in ethyl acetate and washed with water, dried ($MgSO_4$), filtered and concentrated. Chromatography (20% ethyl acetate/hexanes) afforded the desired compound (3.1 g 90%).

Step 3 - The above ester was placed in a solution of NaOH (2N):THF:MeOH (1:2:1) and stirred overnight at room temperature. The reaction was acidified with 6 N HCl and the product extracted with ethyl acetate. The organic layers were dried ($MgSO_4$), filtered and concentrated. The solid was triturated with ethanol and stirred for 1 h. The solid was filtered and dried affording the title compound (1.85 g) as a yellow solid. MS: m/z (M-1) 474

Example 70

2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetic acid

The indole prepared in Example 69, step 1, was alkylated with the appropriate alkyl bromide and hydrolyzed as described in Example 69, steps 2 and 3.

MS: m/z (M-1) 520

Example 71

3-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetyl}amino)benzoic acid

Step 1 - To a solution of the acid from Example 69, step 3, (0.810 g) in THF (28 mL) was added CDI. The reaction was stirred 30 min and then ethyl 3-aminobenzoate (0.330 g) was added and the reaction was stirred overnight. The reaction mixture was taken up in ethyl acetate and washed with water, dried ($MgSO_4$), filtered and concentrated. The crude material was triturated with ethanol and stirred for 1 h, filtered and dried. The desired product (0.76 g, 75%) was isolated as a yellow solid.

Step 2 - The above ester was dissolved in NaOH (2N):THF:MeOH (1:2:1) and stirred 4h. The mixturc was acidified with 6 N HCl and extracted with ethyl acetate. The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The crude solid was triturated with ethanol/hexane to afford the title compound (0.48 g, 69%) as a yellow solid.

Example 72

5-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]isophthalic acid

The alkylated indole from Example 70 was coupled to the appropriate amino acid and hydrolyzed as illustrated in Example 71, steps 1 and 2.

MS: m/z (M-1) 683

Example 73

3-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

The alkylated indole from Example 70 was coupled to the appropriate amino acid and hydrolyzed as illustrated in Example 71, steps 1 and 2.

MS: m/z (M-1) 639

Example 74

5-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetyl}amino)-2-[(5-chloro-3-pyridinyl)oxy]benzoic acid

The alkylated indole from Example 69 was coupled to the appropriate amino acid and hydrolyzed as illustrated in Example 71, steps 1 and 2.

Example 75

5-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]-2-[(5-chloro-3-pyridinyl)oxy]benzoic acid

The alkylated indole from Example 70 was coupled to the appropriate amino acid and hydrolyzed as illustrated in Example 71, steps 1 and 2.

Example 76

2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-N-[3-({[(4-methylphenyl)sulfonyl]amino}carbonyl)phenyl]-2-oxoacetamide

To the acid obtained in Example 71 (0.1 g) in CH_2Cl_2 (10 mL) is added THF (5 mL) to help dissolve the compound. EDCI (0.045 g) and DMAP (0.02 g) was added and the mixture was stirred a room temperature of 1 h. p-Toluenesulfonamide (0.04 g) was added and the reaction was stirred overnight. The reaction mixture was take up in ethyl acetate and washed with water, dried ($MgSO_4$), filtered and concentrated. Chromatography (7% MeOH/CH_2Cl_2) afforded the title compound (0.045 g, 40%) as a yellow solid. MS: m/z (M-1) 746

Example 77

2-[5-bromo-1-(cyclopropylmethyl)-1H-indol-3-yl]acetic acid

To 5-bromoindole-3-acetic acid (890 mg, 3.5 mmol) in 1-methyl-2-pyrrolidinone (12 mL) at 0 °C were added $^iPr_2NEt$ (21 mmol) and bromomethylcyclopropane (10.5 mmol). The reaction mixture was heated at 50 °C for 19 h before partitioning between diethyl ether and ice water. After adjusting the pH to 3, the aqueous layer was extracted with diethyl ether. The organic layers were combined, washed with NaH_2PO_4, dried over $MgSO_4$ and evaporated to dryness. Purification on silica gel column (30% EtOAc in hexane) yielded 927 mg (86 % yield) of the product.

Example 78

2-[1-(cyclopropylmethyl)-5-(2-thienyl)-1H-indol-3-yl]acetic acid

To a sealed tube containing 2-[5-bromo-1-(cyclopropylmethyl)-1H-indol-3-yl]acetic acid (100 mg, 0.32 mmol), 2-thiopheneboronic acid (124 mg, 0.97 mmol), $(C_6H_5)_4Pd$ (37 mg, 0.032 mmol), Na_2CO_3 (2.6 mmol) in a mixture of benzene/EtOH/H_2O (5/1/3, 4.5 mL) was heated at 85 °C for 19 h. The mixture was poured onto diethyl ether and adjusted to pH 3 before extracting with diethyl ether. The mixture was washed with NaH_2PO_4, dried over $MgSO_4$ and evaporated to give the crude product which was purified on silica gel column (33% EtOAc in hexane with 1 % HCOOH) to give 79 mg (78% yield) of the product.

Example 79

2-{1-(cyclopropylmethyl)-5-[3-(trifluoromethyl)phenyl]-1H-indol-3-yl}acetic acid

The title compound was prepared according to the procedure described in Example 78 except that 3-(trifluoromethyl)phenylboronic acid was used.

Example 80

2-[5-(1-benzofuran-2-yl)-1-benzyl-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in Example 78 except that 2-[5-bromo-1-benzyl-1H-indol-3-yl]acetic acid and benzo[b]furan-2-boronic acid were used.

Example 81

2-(1-benzyl-5-phenyl-1H-indol-3-yl)acetic acid

The title compound was prepared according to the procedure described in Example 78 except that 2-[5-bromo-1-benzyl-1H-indol-3-yl]acetic acid and phenylboronic acid were used.

Example 82A

5-((E)-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}methylidene)-1,3-thiazolane-2,4-dione

Step 1

The procedure in Example 22 was followed using 3-formyl indole (0.4g, 2.8mmol), sodium hydride (0.102g, 3.0mmol) and the iodide (0.97g, 2.8mmol) in DMF (10ml). Flash chromatography (Hex/EtOAc, 1/1) gave 0.86g (84%) of the desired intermediate.

Step 2

The intermediate from step 1 (0.8 g, 2.2 mmol) and 2.4-thiazolidinedione (0.25, g, 2.2 mmol) was dissolved in toluene (5 mL). Piperidine (0.064 mL, 0.6 mmol) and acetic acid (0.012 mL) were added and the mixture was heated to reflux for 2h. The reaction was allowed to cool to rt, water was added and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine , dried (MgSO4), filtered and concentrated. Flash chromatography (hexane/ ethyl acetate , 3/2) afforded the title compound (0.345 g (33%) as an orange solid.

Example 82 B

4-{[5-((E)-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}methylidene)-2,4-dioxo-1,3-thiazolan-3-yl]methyl}benzoic acid

The procedure in Example 22 steps 1 and 2 were followed to give 0.14g (47% for 2 steps) of the title compound as a yellow powder.

Example 82 C

2-[5-((E)-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}methylidene)-2,4-dioxo-1,3-thiazolan-3-yl]acetic acid

The procedure in Example 22 steps 1 and 2 were followed to give 0.107g (42% for 2 steps) of the title compound as a yellow powder.

Example 83

3-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}propanoic acid

The procedure in Example 22 step 1 was followed except 2 eq. of sodium hydride was used and 0.142g (65%) of the title compound was isolated as a white oily solid.

Example 84

3-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}propanoic acid

Step 1

To a solution of the aldehyde from Example 114, step1 (1.0g, 2.8mmol) in toluene (20ml) was added carbomethoxyethylidene triphenylphosphorane (0.98g, 2.9mmol). The mixture was heated overnight at reflux and then concentrated. The residue was dissolved in CH_2Cl_2 and silica gel was added. The mixture was concentrated and the resulting solid was purified by flash chromatography (Hex/EtOAc, 3/1). Compound **30** 1.01g (88%) was isolated as a yellow solid.

Step 2

To a solution of the above intermediate (0.1g, 0.24mmol) in THF (10ml), was added platinum on activated carbon (5% Pt, 0.05g, 50 wt%). Hydrogen gas was bubbled into the suspension for 2min, the vessel was sealed tightly and the reaction was stirred overnight at rt. Argon gas was then bubbled through the reaction for 15min before the mixture was filtered through a pad of Celite. The pad was washed with EtOAc and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (5ml). Aqueous saturated $NaHCO_3$ (3ml) was added, followed by cyclopentanecarbonyl chloride (0.036ml). The biphasic mixture was stirred for 2h at rt and diluted with CH_2Cl_2. The organic layer was washed with water and brine, dried and concentrated to a white solid. Recrystallization from EtOAc/Hex gave 0.11g (95%) of the desired intermediate as a white solid.

Step 3

Hydrolysis of the above ester with NaOH (1N, 2 mL) in THF (2mL) and MeoOH (2 mL) followed by recrystallization from hot EtOAc afforded 0.054g (50%) of the title compound as a white solid.

Example 85

N-(1-benzhydryl-3-{3-[(methylsulfonyl)amino]-3-oxopropyl}-1H-indol-5-yl)cyclopentanecarboxamide

To a solution of the acid from Example 84 step 3 (0.1g, 0.22mmol) in THF (5ml) was added methanesulfonamide (0.027g, 0.28mmol), EDCI (0.54g, 0.28mmol) and DMAP (0.012g, 0.1mmol). The mixture was heated at 50°C overnight then diluted with EtOAc, washed with water and brine, dried and concentrated. Flash chromatography (Hex/EtOAc, 1/1) gave 0.1g (87%) of the title compound as a white solid.

Example 86 A

(E)-3-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-propenoic acid

Step1 The same procedure as Example 84 step 2 was used to prepare the desired intermediate from the nitroindole (Example 114 step 1).

Step 2 The procedures in Example 84, step 1 and 3 were used to prepare the title compound from the above intermediate.

Example 86 B

N-(1-benzhydryl-3-{(E)-3-[(methylsulfonyl)amino]-3-oxo-1-propenyl}-1H-indol-5-yl)cyclopentanecarboxamide

The acid from Example 86A was used to prepare the title compound according to the procedure in example 85.

Example 87A

(E)-3-{1-benzhydryl-5-nitro-1H-indol-3-yl}-2-propenoic acid

The ester from Example 84 step 1 was saponified according to the procedure in Example 84 step 3 and recrystallization from hot EtOAc afforded 0.155g (90%) of the title compound as a white solid.

Example 87B

N-((E)-3-{1-benzhydryl-5-nitro-1H-indol-3-yl}-2-propenoyl)methanesulfonamide

The procedure in Example 85 was used to prepare the title compound from the product of Example 87A.

Example 88

4-[(1-benzhydryl-5-chloro-2-methyl-1H-indol-3-yl)methyl]benzoic acid

Step 1 To an ice-cold ($0^{0}C$) solution of trifluoroacetic acid (1.7ml, 15mmol) and triethylsilane (4.8ml, 30mmol) in CH_2Cl_2 (20mL) was added a solution of 5-chloro-2-methylindole (1.66g, 10mmol) and methyl 4-formylbenzoate (1.8g, 11mmol) in CH_2Cl_2 (50mL) over a period of 5 min. The resulting homogeneous solution was stirred at $0^{0}C$ for 1h and rt for 2h, at which time EtOAc (150mL) and aqueous sodium bicarbonate (to pH=8) was added. The organic layer was washed with water and brine, dried over $MgSO_4$ and concentrated. Flash chromatography (Hex/EtOAc, 4/1) gave 1.98g (63%) of desired intermediate as a light-tan solid.

Step 2 Sodium hydride (0.2g, 5mmol) was washed with dry hexanes (3x10ml) and then suspended in DMF (6mL) and cooled to 0^{0}C. A solution of the above intermediate (1.57g, 5mmol) in DMF (4mL) was dropwise at 0^{0}C and the resulting mixture was stirred for 30min at which time the diphenylbromomethane (1.24g, 5mmol) was added. The mixture was allowed to reach rt and stirred for an additional 48h. EtOAc (30mL) was added followed by aqueous NaH_2PO_4 solution (10ml). The organic layer was washed with water and brine, dried and concentrated. Flash chromatography (Hex/EtOAc, 7/1) provided 0.98g (41%) of the desired intermediate as a ivory foam.

Step 3

The above intermediate was saponified according to the procedure in Example 84 step 3. Flash chromatography (EtOAc) provided 0.3g (89%) of the title compound as a tan crystalline solid. MS: m/z (M-1) 464

Example 89

4-{[1-benzhydryl-5-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step1 - The intermediate from Example 3 step 2 (1eq) (see scheme #) was weighed in to a flask along with the 4-trilflouromethylbenzene sulfonyl chloride (1.2 eq) and then they were flushed with nitrogen, taken up in dichloroethane (0.15 M) and then pyridine was added (1.2 eq) at which time the reaction was left to stir overnight and then worked up by the addition of the polymer bound amine (Parlow, J.J, Mischke, D. A., Woodard, S.S.*J. Org. Chem.* **1997**, *62*, 55908-5919) (1.6g/1mmol) and the resulting slurry was stirred a minimum of 15 minutes and then it was filtered and washed with dichloroethane and the dichloroethane solution was dried and concentrated to yield 98% of the desired product with high purity.

Step 2 - The crude material from step1 was dissolved THF/MeOH (2.5/1) and then 4N NaOH was added (3 eq) and the reaction was stirred until complete hydrolysis was observed by TLC. At this point the reaction quenched with enough amberlite ir 120 to make the solution acidic and then the resin was filtered off and rinsed and the desired product was obtained in 94% yield by drying and concentrating the solution. MS: m/z (M-1) 669

Example 90

4-{[5-({[2-(acetylamino)-4-methyl-1,3-thiazol-5-yl]sulfonyl}amino)-1-benzhydryl-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 76% of the title compound after chromatographic purification.

Step 2: An analogous proceedure to step 2 for Example 89 above yielded 83% of the desired product. MS: m/z (M-1) 679

Example 91

4-[(1-benzhydryl-5-{[(4-chloro-3-nitrophenyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 100% of the title compound.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 54% of the desired product after chromatographic purification. MS: m/z (M-1) 681

Example 92

4-[(1-benzhydryl-5-{[(dimethylamino)sulfonyl]amino}-1H-indol-3-yl)methyl]-3- Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 49% of the title compound after chromatographic purification.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 100% of the desired product. MS: m/z (M-1) 568

Example 93

4-{[1-benzhydryl-5-({[4-(trifluoromethoxy)phenyl]sulfonyl}amino)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 100% of the title compound.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 100% of the desired product. MS: m/z (M-1) 685

Example 94

4-[(1-benzhydryl-5-{[(2-methylphenyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 56% of the title compound after chromatographic purification.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 82% of the desired product. MS: m/z (M-1) 615

Example 95

4-[(1-benzhydryl-5-{[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 100% of the title compound.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 96% of the desired product.

MS: m/z (M-1) 655

Example 96

4-[(1-benzhydryl-5-{[(3,5-dimethyl-4-isoxazolyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1: Following step 1 for Example 89 using the appropriate sulfonyl chloride yielded 100% of the title compound.

Step 2: An analogous proceedure to step 2 for Example 89 yielded 89% of the desired product.

MS: m/z (M-1) 621

Example 97

Cyclopentyl-N-{3-[4-(aminocarbonyl)-2-methoxybenzyl]-1-benzhydryl-1H-indol-5-yl}carbamate

The compound of Example 3 (1.0 eq) was dissolved in THF (0.15M) and then carbonyl diimidizole (1.2 eq) was added and the reaction was stirred under N_2 for three hours at which time ammonium hydroxide was added (3ml/g) and the reaction was stirred overnight when TlC analysis showed it was complete. To the reaction was added water and ethyl acetate, the layers were separated and the aqueous layer was extracted three times, the combined organic extracts were dried concentrated and chromatographed to yield 64% of the desired primary amide.

Example 98

cyclopentyl N-{1-benzhydryl-3-[2-methoxy-4-(1H-1,2,3,4-tetraazol-5-yl)benzyl]-1H-indol-5-yl}carbamate

Step 1 - To the compound of Example 97 (1.0 eq) under N_2 was added CH_2Cl_2 (0.06M) and then (methoxycarbonylsulfamoyl)triethylammonium hydroxide inner salt (5.0 eq) portion wise over 5 hours and then the slurry was stirred overnight at which time TLC analysis indicated the reaction was complete so it was concentrated and chromatographed to yield 78% of the desired product.

Step 2 - To the nitrile (1.0 eq) isolated in step 1 was add sodium azide (3 eq) and triethyl amine hydrochloride (1.5 eq) and n-methyl-2-pyrrolidinone (0.05m) and then the reaction was heated to reflux under an inert atmosphere for 2.5 hours when it was poured into ice and water that was then acidified to pH 2 and the product was filtered off and then further purified by preparative chromatography to yield the desired compound in 22% yield. MS: m/z (M-1) 597

Example 99

4-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]-3-thiophenecarboxylic acid

step 1 To the indole acid (1.0 eq) was added the amine (1.2 eq) the dimethylaminopyridine (10 mol %), 1-(3dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.5 eq) and then DMF(0.3M) and the reaction was stirred under nitrogen for 24 hours at 40°C for 24 hours at which time it was poured into 1/2 saturated ammonium chloride solution and ethyl acetate and then the layers were separated and the aqueous layer was extracted 3 times, the combined organic layers were washed with water 2X, dried, concentrated and chromatographed to yield 38% of the amide.

Step 2 The ester from the previous step was dissolved in THF/MeOH (3:1) and then 1N NaOH (3.0eq) was added and the reaction was stirred for until TLC analysis showed that the reaction was complete. The reaction was then concentrated, diluted with water, acidified to pH 2 with conc HCL, extracted with ethyl acetate 3X, the combined organics were dried over magnesium sulfate concentrated and purified via chromatography to yield the desired acid in 64% yield.

Example 100

3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]benzoic acid

Step 1: The acid (see scheme #) was coupled with the appropriate amino ester following the procedure in Example 99, step one, except the reaction was run at room temperature and that the procedure yielded 80% of the desired product isolated by recrystalization.

Step 2: The nitro ester from step one (1.0 eq) was weighed into a flask along with 5% Platinum on Carbon (40 wt%) and the vessel was sealed with a septum and evacuated and flushed with argon 3X, then freshly distilled THF is added and the reaction is evacuated 2X and after the second evacuation a balloon of hydrogen inserted into the septum. The reaction is left under atmospheric hydrogen for 16 hours at which time tlc analysis indicates complete reduction and the reaction is flushed with argon and then filtered through a bed of celite and the catalyst is

washed exhaustively with ethyl acetate, the filtrate was dried and concentrated and purified via chromatography to deliver 71% of the desired amine.

step 3: The amine (1.0 eq) was dissolved in dichloromethane (0.3M) and then an equivalent amount of saturated sodium bicarbonate was added and finally the acid chloride introduced. The biphasic reaction mixture was vigorously stirred until TLC analysis indicated that the reaction was complete (generally a few hours) and then the reaction was diluted with dichloromethane and water, the layers were separated, the aqueous layer was extracted three times with dichloromethane, the combined organic layers were dried, concentrated and chromatographed to yield the desired amide in 41% yield.

Step 4:

According to step 2, Example 99, the ester was hydrolyzed to the acid and yielded 71% of the final product. MS: m/z (M-1) 556

Example 101

3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]propanoic acid

step 1 To the final product in Example 114 (1.0eq) in dichloromethane (0.1M) at 0°C was added oxallyl chloride (2.0 eq) and then a few drops of DMF. The reaction was stirred a few hours at room temperature and concentrated and azeotroped 2X with toluene and placed on the high vacuum for 2 hours before being used crude for the next step.

Step 2: To the acid chloride generated in step 1 was added dichloromethane (0.1M) and then a solution of alanine methyl ester (1.05eq, free base) in dichloromethane (1.0M) and then triethylamine (1.5eq)was added and the resulting mixture was stirred overnight and worked up by the addition of 1/2 saturated ammonium chloride, the layers were separated, the aqueous layer was extracted three times with dichloromethane, the combined organic layers were dried and concentrated and purified via chromatography to yield the desired amide.

Step 3: The ester from step 2 was hydrolyzed under the conditions outlined for step 2, Example 99, to yield the desired acid.

Example 102

N-[1-benzhydryl-3-({[(2-methylphenyl)sulfonyl]amino}carbonyl)-1H-indol-5-yl]cyclopentanecarboxamide

Step 1: The acid chloride (1.0 eq) synthesized in step 1, Example 101, was weighed into a flask along with o-tolylsulfonamide (1.5eq), DMAP (0.1 eq) and taken up in dichloromethane (0.1M) under nitrogen and then triethylamine (1.5eq) was added and the resulting mixture was stirred for 12 hours and then worked up by the addition of 1/2 saturated ammonium chloride,

the layers were separated, the aqueous layer was extracted three times with dichloromethane, the combined organic layers were dried and concentrated and purified via chromatography to yield the desired acylsulfonamide in 52% yield.

Example 103

3-[(2-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-oxoacetyl)amino]propanoic acid

Step 1: According to the general procedure in step 1, Example 101, using the product from Example 115 and the appropriate amino ester yielded the desired product in 100% yield.

Step 2: The ester from step 1 was hydrolyzed under the conditions outlined for step 2, Example 99, to yield the desired acid. MS: m/z (M-1) 536

Example 104

3-[(2-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1: According to the general procedure in step 1, Example 99, using the product from Example 115 and the appropriate amino ester yielded the desired product in 100% yield.

Step 2: The ester from step 1 was hydrolyzed under the conditions outlined for step 2, Example 99, to yield the desired acid. MS: m/z (M-1) 584

Example 105

3-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]acetyl}amino)benzoic acid

Step 1

An oven dried flask was charged with 5-benzyloxy indole-3-acetic acid (1 eq) (see scheme-1) and anhydrous DMF (0.18 M) under nitrogen. Reaction mixture was then cooled to 0°C and to this was added NaH (2.2eq, 60% dispersion in mineral oil), stirred at 25°C for 1h followed by addition of a solution of the appropriate benzyl bromide (2.2eq, 40% purity) (see scheme-1, steps 5,6) in anhydrous DMF, stirred overnight. Workup with ethyl acetate/water followed by chromatographic purification afforded the desired product in 66% yield.

Step 2

Dissolved the indole derivative from step 1(1 eq) (see scheme-1) in THF/MeOH/H_2O (3:1:1 0.094 M) and to this was added $LiOH{\cdot}H_2O$ (1.2 eq), stirred at 25°C, overnight. Workup with ethyl acetate/water followed by chromatographic purification afforded the desired product in 74% yield.

Step 3

To the acid from step 2 (1 eq) (see scheme-1) was added methyl 3-aminobenzoate (1.05 eq), EDCI (1.37 eq) and DMAP (0.2 eq) followed by anhydrous DMF (0.086M), stirred at 25°C, overnight. Workup with ethyl acetate/1N HCl followed by chromatographic purification afforded the desired product in 80% yield.

Step 4

Dissolved the ester (1 eq) from step 3 (see scheme-1) in THF/MeOH/H_2O (3:1:1 0.04 M) and to this was added LiOH·H_2O (1.2 eq), stirred at 25°C, overnight. Workup with ethyl acetate/1N HCl followed by trituration with CH_2Cl_2/hexane (1:1) for 0.5h and then recrystallization from CH_2Cl_2 afforded the titled product in 97% yield. MS: m/z (M-1) 579

Example 106

3-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}acetyl)amino] benzoic acid

Step 1

Following procedure in step 1 of example 105, scheme-1 and using the appropriate benzyl bromide afforded the desired product in 50% yield after chromatographic purification.

Step 2

Following procedure in step 2 example 105, scheme-1 and using the appropriate indole derivative afforded the desired product in 67% yield after chromatographic purification.

Step 3

Following procedure in step 3 example 105, scheme-1 and using the appropriate indole derivative afforded the desired product in 75% yield after chromatographic purification.

Step 4

Following procedure in step 4 example 105, scheme-1 and using the appropriate indole afforded the desired product in 63% yield after chromatographic purification.

MS: m/z (M-1) 625

Example 107

5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-2-methyl-1H-indole-3-carboxylic acid

Step 1: The 5-Hydroxy-2-Methylindole-3-Carboxylate (1 eq) was combined with benzyl bromide (1.3 eq) and K_2CO_3 (325 mesh, 1.3 eq) in CH_3CN (0.1 M). The resulting mixture was heated to reflux for 2 h. An additional amount of benzyl bromide (0.2 eq) and the heating was continued for 2 h. The reaction was worked up by addition of water and extraction with CH_2Cl_2. The organic extracts were washed with water, dried and concentrated. Flash

chromatography provided the desired benzyl ether (63 % yield), as well as the corresponding N,O-bisbenzyl derivative (22 % yield).

Step 2: An ice cooled solution of the benzyl ether from step 1 (1 eq) in dry DMF (0.25 M) was treated with NaH (60 % in mineral oil, 1.1 eq). 2,4-Bis trifluoromethyl benzyl bromide (1.1 eq) was added after 1 h and the resulting mixture was stirred at 25°C for 2 h. Solvent was evaporated under vacuo, the residue was dissolved in EtOAc, washed with water, dried and concentrated. The desired product was obtained in 77 % yield after recrystallization from hexane/$CHCl_3$.

Step 3: The product from step 2 (1 eq) in THF/MeOH (3/1) was heated to reflux with 1N NaOH (12 eq). After 48 h the reaction was quenched with AcOH and solvent was evaporated. The resulting product was recrystallized to afford crude material in 72 % yield. Further purification by flash chromatography followed by recrystallization provided pure title compound. MS: m/z (M-1) 506

Example 108

5-[({5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-2-methyl-1H-indol-3-yl}carbonyl)amino]isophthalic acid

Step 1: The acid prepared in step 3 (1 eq) of example 108 was reacted with EDCI (2 eq) and dimethyl 5-aminophthalate (5 eq) in THF (0.02 M) in the presence of DMAP (2 eq). The reaction was heated to reflux for 48 h. EtOAc/water work up, followed by flash chromatography produced the desired amide in 32 % yield.

Step 2: The material from step 1 (1 eq) was hydrolyzed by the action of $LiOH \cdot H_2O$ (2.2 eq) in THF/MeOH/water (3/1/1, 0.07 M). After stirring at 25°C overnight, the reaction mixture was quenched with AcOH and solvent was evaporated. EtOAc/water work up and trituration in hexane/CH_2Cl_2 afforded the title compound in 82 % yield. MS: m/z (M-1) 669

Example 109

5-(benzyloxy)-2-methyl-1-(2-naphthylmethyl)-1H-indole-3-carboxylic acid

Step 1: An analogous procedure to step 2 example 108 using the main product of step 1 above and the appropriate bromide yielded the desired N-substituted indole in 71 % yield after recrystallization.

Step 2: The ester from step 2 above (1 eq) in THF/MeOH (3/1) was heated to reflux with 4N KOH (2 eq). After 5 days solvent was evaporated and the residue partitioned between 1N HCl and $CHCl_3$. The organic extract was washed, dried and concentrated. The title compound was obtained in 92 % yield after chromatographic purification and crystallization. MS: m/z (M-1) 420

Example 110

5-({[5-(benzyloxy)-2-methyl-1-(2-naphthylmethyl)-1H-indol-3-yl]carbonyl}amino)isophthalic acid

Step 1: The acid in Example 109 was converted in the corresponding amide following an analogous procedure to step 1 of Example 108. The product was contaminated with the aniline starting material which could only be partially removed by chromatography.

Step 2: Hydrolysis of the crude material following step 2 Example 108 provided the title compound after chromatographic purification (4 % yield in Example 109).

Example 111

1-benzyl-5-(benzyloxy)-2-methyl-1H-indole-3-carboxylic acid

Step 1: The minor product of step 1 (1 eq) Example 107 was dissolved in THF (0.1 M). KOH (2 eq) and 18-crown-6 (2 eq) were added and the resulting mixture was heated to reflux for 1.5 days. Work up as on step 2 Example 108 above provided the title compound in 32 % yield. MS: m/z (M-1) 370

Example 112

3-[(2-{5-(benzyloxy)-1-(4-chlorobenzyl)-2-[(2-naphthylsulfanyl)methyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1 The starting ethyl 5-benzyloxyindole-2-carboxylate (Scheme 21, step 1) was treated with LAH (1.3 eq) in THF (0.27 M) at 0 °C under nitrogen for 1 h. Workup with NaOH and water followed by concentration afforded crude product (100%).

Step 2 The crude alcohol from step 1 was dissolved in DMF (0.38 M), and treated with t-butyldimethylsilyl chloride (1.16 eq) and imidazole (1.26 eq) at 25 °C for 1 d. Workup and chromatographic purification afforded the pure product (93%).

Step 3 The silyl ether from step 2 was dissolved in methylene chloride (0.26 M), and treated with BOC anhydride (1.24 eq), triethylamine (1.53 eq) and DMAP (0.21 eq) at 25 °C for 3 d. Workup and chromatographic purification afforded the pure product (99%).

Step 4 The N-BOC silyl ether from step 3 was treated with acetic acid/ water/ THF (3:1:1) (0.04 M) at 25 °C for 1 d. Workup and chromatographic purification afforded the pure product (100%).

Steps 5 The alcohol from step 4 was dissolved in methylene chloride (0.2 M), and under nitrogen at -40°C treated with triethylamine (1.33 eq), and mesyl chloride (1.23 eq) for 1 h. In a separate dry flask was weighed naphthalene-2-thiol (1.31 eq), and THF (1 M) was added, followed by lithium hexamethyldisilazide (1N in THF, 1 eq) and this mixture was

stirred at 25°C for 30 min. The resulting solution was then added dropwise, over 30 minutes, to the above mesylate solution, at -40°C. The reaction mixture was allowed to warm to 25°C, and stirred there for 4.5 h. Workup and chromatographic purification afforded the BOC thioether.

Step 6 The purified BOC thioether from step 5 was heated under nitrogen at 160-170°C for 1.25 h, and recrystallized from ethyl acetate and hexanes to afford the free indole thioether in 64% yield.

Step 7 The indole thioether from step 6 was dissolved in DMF (0.2 M), and treated with sodium hydride (1.1 eq) at 25°C for 45 min. 4-Chlorobenzyl chloride (1.3 eq) and KI (cat.) were added, and the mixture was stirred at 25°C for 3 d. Workup (ethyl acetate/water) and trituration (ethyl acetate/hexanes) afforded the pure product (52%).

Step 8: A solution of EtMgBr in ether (3 N, 2.17 eq) was cooled to - 70 °C. The product of step 7 in scheme 21 (1 eq) in ether (0.55 M) was added and the reaction mixture was stirred at -70 °C for 2 h. After the addition of methyl oxalyl chloride (3 eq) in ether (1.5 M) the reaction was stirred at - 40 °C for 2 h, allowed to warm to 25 °C. Quenched with sodium bicarbonate EtOAc/water work up and crystallization from hexane/EtOAc the desired ketone.

Step 9 The ester from step 8 was hydrolyzed using the general method in step 2 example 108 to yield the desired alpha keto acid.

Step 10 The indole thioether from step 9 was dissolved in dry methylene chloride (0.05 M), and treated with oxalyl chloride (2.05 eq) at 0°C for 1 h. In a separate dry flask were weighed 3-aminobenzoic acid (10 eq) and triethylamine (15 eq) in methylene chloride (0.5 M). The resulting solution was then added dropwise, at 0°C, and the mixture was allowed to warm to 25°C overnight. Workup (methylene chloride/aqueous HCl) and repeated purification by chromatography afforded the pure title compound product.

Step 11 The product from step 9 was hydrolyzed using the procedure from step 2 Example 108 to yield the desired compound in 28%. MS: m/z (M-1) 709

Example 113

3-[(2-{5-(benzyloxy)-1-methyl-2-[(2-naphthylsulfanyl)methyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid

Step 1 Following step 4 of the above procedure using methyl iodide followed by trituration (ethyl acetate/hexanes) afforded the pure product (72%).

Step 2 An analogous procedure to step 5 through step 11 above yielded 58% of the title compound. MS: m/z (M-1) 599

Example 114

1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indole-3-carboxylic acid

Step 1 5-nitroindole was alkylated as in Example 3 step1 with the appropriate bromide to yield the desired N-alkylated product.

Step 2 The indole from step 1 (1.0eq) was dissolved in DMF (0.4M) and treated with phosporous oxychloride (6.9 eq) at room temperature and then the mixture was stirred for 1 day at 80 C at which time the reaction was poured onto ice and triturated with ethyl acetate/hexanes, followed by workup with sodium bicarbonate/chloroform yielded the C3 formylated product.

Step 3 The nitro indole from step 2 was reduced according to the procedure in Example 100, step 2 to yield the amino aldehyde.

Step 4 The indole from step 3 was acylated according to the procedure from Example 100, step 3.

Step 5 The indole from step 4 (1.0 eq), 2 methyl-2butene (45 eq), sodium dihydrogen phosphate (11.6 eq). were dissolved in t-BuOH (0.2M), water (0.2M) and then sodium chlorite (11.6q) was added and the reaction was heated to 65 C for 24 hours.The reaction was diluted with water, extracted 3 times with ethyl acetate, dried and concentrated and then purified by chromatography to yield the title compound.

Example 115

2-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-oxoacetic acid

Step 1 Following the procedure of Example 69, 5-niroindole was acylated in the 3-position with ethylmagnesiumbromide and ethyloxalylchloride.

Step 2 The above intermediate was elaborated to the final product following steps 2-5 of Example 114 to afford the title compound.

Example 116

Table I reports data for the compounds described in the examples above in cPLA2 inhibition assays (described below). In the data columns of Tables I and II, assay results are reported as a percent inhibition at the concentration specified.

Coumarin Assay

7-hydroxycoumarinyl 6-heptenoate was used as a monomeric substrate for cPLA2 as reported previously (Huang, Z. et al., 1994, Nalytical Biochemistry 222, 110-115). Inhibitors were mixed with 200 μL assay buffer (80 mM Heped, pH 7.5, 1 mM EDTA) containing 60 μM 7-hydroxycoumarinyl 6-heptenoate. The reaction was initiated by adding 4 μg cPLA2 in 50 μL assay buffer. Hydrolysis of the 7-hydroxycounarimyl 6-heptenoate ester was monitored in a fluorometer by exciting at 360 nm and monitoring emission at 460 nm. Enzyme activity is proportional to the increase in emission at 460 nm per minute. In the presence of a cPLA2 inhibitor, the rate of increase is less.

Table I

Example	PERCENT INHIBITION @	CONCENTRATION (micromolar)
1	7	50
	18	100
	50	170
2	50	25
	50	32
3	50	5
	51	6.25
	50	6.4
	41	10
	50	17.5
	50	19
	37	20
	38	20
	43	20
	44	20
	50	20
	50	20
	50	22
	50	23
	50	23.5

	50	24
	39	100
	50	5
	51	6.25
4	50	5
	50	11
	50	5
	50	11
5	41	100
	50	120
6	11	100
	50	200
7	11	50
	50	235
8	50	65
	44	100
9	50	13
	50	19
10	50	20
	50	20
	50	30
	50	33.5
	50	40
	50	45
11	42	10
	50	12
	52	12.5
	36	20
	50	27.5
	50	30
	50	30
	50	37
12	50	0.35
	50	0.35
	50	0.38
	50	0.38
	50	0.38
	50	0.39
	50	0.4
	50	0.4
	50	0.4

	50	0.44
	50	0.45
	64	0.5
	86	1.25

13	50	0.39
	50	0.4
	50	0.48
	50	0.55
	50	0.6
	50	0.65
	50	0.65
	50	0.7
	50	0.75
	50	0.95
	73	2.5
	81	6.25

14	50	0.7
	50	0.95
	50	0.95

15	50	0.65
	50	0.65
	50	0.72
	50	0.76
	50	0.85
	90	6.25

16	50	0.125
	61	0.125
	71	0.125
	50	0.14
	50	0.14
	50	0.14
	50	0.17
	50	0.17
	69	0.25
	98	6.25

17	50	0.7
	50	0.8
	50	0.85
	50	0.98

18	50	1.2
	50	1.3
	50	1.9
	50	2
	50	2

	50	2
19	50	2.2
	50	4.2
	50	5.8
	52	6.25
	50	7.8
	50	9
	50	11
	50	12
20	50	25
	50	32
21	50	20
	50	20
22	50	38
	50	40
23	50	10
	58	20
24	42	100
	50	100
25	50	13
	50	17
26	50	2.4
	50	2.5
27	50	6
	50	6.4
28	50	4.2
	50	4.4
29	50	2.5
	50	3.4
	87	6
30	50	8
	46	20
	50	21
	50	24
31	50	11
	50	18

32	50	4
	50	4.4

33	50	4.4
	50	4.9

34	50	2
	57	2.5

35	23	10
	42	20
	50	41

36	50	0.22
	60	0.25
	50	0.32
	50	0.45

37	50	0.4
	50	0.5
	50	0.55
	50	0.65

38	50	0.3
	50	0.45
	50	0.57
	50	0.59
	50	0.6
	50	0.6
	50	0.6
	50	0.6
	50	0.6
	50	0.64
	50	0.7
	50	0.7
	50	0.85
	50	0.85
	50	1
	50	1

39	50	0.39
	50	0.7
	50	0.73
	50	0.75
	50	0.75
	50	0.8
	50	0.9
	50	0.9
	50	1
	50	1

	50	1.2
	50	1.3
	50	1.6
40	50	2.5
	55	2.5
	50	3
	50	3.6
41	50	2.5
	50	3.8
	50	4.3
	50	5
42	50	2.2
	50	3
	50	3.8
43	50	12
	50	14
44	50	1.65
	50	1.7
	50	1.75
	50	1.9
	50	2.1
	71	2.5
	97	6.25
45	50	1.75
	50	1.8
	50	1.9
	50	2
	50	2.1
	74	2.5
46	50	2.2
	67	2.5
	50	2.7
	50	3.5
	50	4.5
49	50	1.5
	50	1.8
	50	2.3
50	50	0.8
	50	0.8
	50	0.85
	50	1.05

	81	2.5
51	50	0.6
	50	0.8
	50	0.9
52	50	19
	50	19
	50	20
53	50	11
	50	15.5
54	50	2.8
	50	3.9
55	50	1.35
	50	1.35
56	50	0.98
	50	1.2
57	50	1.05
	50	1.38
	50	1.4
58	50	1.65
	50	1.65
59	50	6
	90	12.5
60	50	12.5
61	50	10
	54	12.5
62	50	7
	86	12.5
63	70	2.5
	50	7
64	50	32
	50	37
65	47	50
	50	72
	50	80

66	50	70
	15	200
	19	200
67	8	100
	31	400
68	9	100
	18	400
69	50	12.5
70	39	50
	40	50
71	69	6
	50	1.5
	50	3.5
	50	3.8
72	50	12.5
76	50	4
77	50	160
	50	180
78	50	80
	50	110
79	50	60
	50	65
80	50	48
	60	50
81	50	70
	46	100
82A	50	46
	50	50
82B	61	6.25
	50	6.5
82C	50	8
	50	10
83	50	48
	50	70

84	22	100
	50	265
	50	350
85	31	100
	50	200
86A	50	60
	50	70
	50	82
	50	118
86B		
87A	33	50
	50	95
87B	50	38
	50	38
	50	42.5
88	50	1.25
	53	1.25
	50	1.32
89	50	4.4
	50	4.8
90	50	10.2
	50	10.5
91	50	3.8
	50	4.25
92	50	11
	50	12.5
	50	14.2
93	50	4.2
	50	4.9
94	50	7
	50	7.5
95	50	11.5
	50	13
96	50	8
	50	10.5

97	50	50
	50	80
	50	94

98	50	4.8
	66	6.25
	50	8.7

99	13	30
	38	100
	50	100
	50	100

100	50	24
	50	30
	50	80

101	6	100
	49	400

102	31	20
	50	48

103	50	100
	50	104

104	50	22
	50	24

105	50	2.4
	50	7
	74	10

106	50	7
	50	12

107	50	80
	50	71
	43	50
	50	37
	50	37

108	67	6.25
	15	20
	50	48
	46	50
	46	50

109	28	50

	25	50
110	50	47
	50	46
111	16	50
	15	50
112	53	2.5
113	50	7.5
	50	8
114	45	100
	50	152
	50	170
115	89	50
	20	100
	50	250
117	50	1.6
118	50	0.6
119	50	2.5
120	50	1
121	20	1.6
122	64	1.25
123	50	1.2
124	50	1.3
125	50	0.8
126	50	5.5
127	50	1.1
128	50	0.9
129	50	1.1
130	50	2
131	50	0.6

132	50	0.4
133	50	0.3
134	50	0.8
135	50	0.7
136	50	0.4
137	50	0.8
138	50	0.4

Compounds of the present invention were also tested for *in vivo* activity in a rat paw edema test according to the procedure described below. The results are reported in Table II.

Rat Carrageenan-Induced Footpad Edema Test

Each compound was suspended in 0.3ml absolute ethanol, 0.1 ml Tween-80 and 2.0 ml Dulbecco's PBS (without calcium or magnesium). To this mixture, 0.1ml 1N NaOH was added. After solution was complete, additional amounts of PBS were added to adjust the concentration to 1 mg/ml. All compounds remained in solution. Compounds were administered i.v. in a volume of 5 ml/kg to male Sprague Dawley rats at the same time that edema was induced by injection of 0.05ml of 1% Type IV carrageenan into the hind footpad. Footpad volume was measured before dosing with compound and 3 hours after dosing with carageenan.

Table II

Example	ROUTE of ADMIN.	DOSE (mg/Kg)	PERCENT INHIBITION
1	IV	5	2.51
	IV	5	16.61
2	IV	5	15.87
3	IV	5	10.38
	PO	5	21.5
	IV	5	22.84
	IV	5	14.86
	PO-	20	19.56
	IV	5	10.38
4	IV	5	24.13
	IV	5	4.95
5	IV	5	8.88
	IV	5	24.28
	IV	5	0.09
7	IV	5	-0.65
8	IV	5	-5.7
9	IV	5	4.46
10	IV	5	25.32
11	IV	5	13.98
12	PO	2	0.19
	PO	10	-0.38
13	PO	2	25.99
	PO	10	23.63
14	PO	2	11.53
	PO	10	8.14
15	PO	2	7.05
	PO	10	6.88
16	PO	2	3.8
	PO	10	14.96

17	PO	2	19.29
	PO	10	34.52

19	IV	5	21.17
	IV	5	13.32
	IV	5	-0.09

21	IV	5	16.18
	IV	5	19.01
	IV	5	8.66

22	IV	5	9.22
	IV	5	4.14

23	IV	5	15.71
	IV	5	14.45
	IV	5	2.12

24	IV	5	8.33
	IV	5	16.28
	IV	5	11.3

25	IV	5	2.73
	IV	5	8.66
	IV	5	16.02

26	IV	5	25.31

27	IV	5	6.48

28	IV	5	0.29

30	IV	5	13.89
	PO	2	-0.11
	PO	10	13.25

37	PO	2	-7.94
	PO	10	3.36

38	PO	2	15.44
	PO	10	26.32

39	PO	2	1.98
	PO	10	-7.16

40	IV	5	8.21

41	IV	5	10.1

42	IV	5	7.72

44	IV	5	11.9
45	IV	5	10.19
46	IV	5	4.58
49	IV	5	18.02
50	PO	2	5.44
	PO	10	12.34
51	PO	2	3.23
	PO	10	15.37
52	PO	2	-6.75
	PO	10	3.33
53	PO	2	-1.81
	PO	10	11.35
54	PO	2	2.47
	PO	10	14.29
55	PO	2	7.02
	PO	10	21.51
56	PO	2	4.22
	PO	10	9.34
57	PO	2	10.44
	PO	10	20.68
58	PO	2	13.85
	PO	10	9.96
59	IV	5	2.9
61	IV	5	18.33
63	IV	5	19.59
65	IV	5	2.84
66	IV	5	25.34
67	IV	5	10.78
68	IV	5	-4.3

76	IV	5	14.84
80	IV	5	10.18
82B	IV	5	4.94
84	IV	5	6.15
85	IV	5	7.13
86A	IV	5	7.4
87A	PO	2	12.89
	PO	10	25.44
87B	PO	3	17.92
	PO	10	31.4
89	PO	2	14.34
	PO	10	16.38
90	PO	2	-0.18
	PO	10	2.7
91	PO	2	13.5
	PO	10	14.67
92	PO	2	27.36
	PO	10	21.34
93	PO	2	-3.02
	PO	10	9.91
94	PO	3	3.13
	PO	10	4.46
	PO	2	19.04
	PO	10	27.45
95	PO	2	14.86
	PO	10	23.19
96	PO	2	29.42
	PO	10	21.99
97	IV	5	21.31
98	IV	5	18.39
99	PO	10	22.77
	PO	2	24.51

100	PO	2	6.14
	PO	10	20.7

101	PO	10	12.45
	PO	2	11.17

102	PO	2	2.56
	PO	10	8.48

103	PO	10	17.31
	PO	2	16.5

104	PO	2	14.49
	PO	10	6.01

105	IV	5	1.51

114	PO	2	12.15
	PO	10	22.19

115	PO	2	1.24
	PO	10	18.46

Example 117

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-2,6-dimethylphenoxy}acetic acid

Step 1: To 1-benzhydryl-6-chloro-1H-indole (1.0 eq) and methyl 2-(4-formyl-2,6-dimethylphenoxy)acetate (0.6 eq) in CH_2Cl_2 (0.1M) at 0°C was added neat triethysilane (3eq) followed by triflouroacetic acid (3eq). After 10 minutes at 0°C the reaction was warmed to room temperature and stirred until the initially formed spot by TLC yields a new spot. The reaction was then quenched by the addition of saturated sodium bicarbonate, diluted with CH_2Cl_2 and washed with saturated sodium bicarbonate, water and brine, dried over magnesium sulfate and purified by column chromatography to yield 89% of the desired product.

Step 2 The resulting ester was hydrolyzed as in example 1 step 5 to yield the title compound after trituration and/or column chromatography. m/z (M-1)508.3

Example 118

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxyphenoxy}acetic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and methyl 2-(4-formyl-3-methoxyphenoxy)acetate according to the procedure in Example 117 Step 1.
Step 2: The ester intermediate was hydrolyzed according to step 2 Example 117 to yield the title acid.

Example 119

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]phenoxy}acetic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and methyl 2-(4-formylphenoxy)acetate according to the procedure in Example 117 Step 1.

Step The ester intermediate was hydrolyzed according to step 2 Example 117 to yield the title acid.

Example 120

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-chlorophenoxy}acetic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and methyl 2-(3-chloro-4-formylphenoxy)acetate according to the procedure in Example 117 Step 1 in 70% yield.
Step 2: The ester intermediate was hydrolyzed according to step 2 Example 117 to yield the title acid.

Example 121

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-2-methoxyphenoxy}acetic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and methyl 2-(4-formyl-2-methoxyphenoxy)acetate according to the procedure in Example 117 Step 1 in 71% yield.
Step 2: The ester intermediate was hydrolyzed according to step 2 Example 117 yield the title acid. m/z (M-1)510.2

Example 122

(E)-4-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]phenoxy}-2-butenoic acid

Step 1: This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and (E)-4-(4-formylphenoxy)-2-butenoate according to the procedure in Example 117 Step 1 in 91% yield.
Step 2:The ester intermediate was hydrolyzed according to step 2 Example 117 to yield the title acid. m/z (M-1)506.3

Example 123

4-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-4-oxobutanooic acid

Step 1 This intermediate compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and 4-nitrobenzaldehyde according to the procedure in Example 117 Step 1 in 42% yield.
Step 2 -benzhydryl-6-chloro-3-(4-nitrobenzyl)-1H-indole was reduced by dissolving in THF (0.1 M), subjecting it to 1 atmosphere of hydrogen gas in the presence of 10%platinum on carbon catalyst (25%w/w). When the starting material had all been converted to a new spot by TLC analysis the reaction was filtered and concentrated to yield the desired intermediate in nearly quantitative yield.
Step 3:To the intermediate above (1.0 eq) in CH_2Cl_2 (0.1M) at 0°C was added triethylamine (1.5 eq) followed by 3-carbomethoxyproprionyl chloride(1.5 eq). The reaction was warmed to room temperature, stirred until complete disappearance of starting material as monitored by TLC, and then worked by the addition of saturated sodium bicarbonate, dilution with CH_2Cl_2, and washing the organic layer with water, saturated sodium bicarbonate and brine, dried, concentration and purified by column chromatography to yield the desired compound in 81% yield.
Step4: The ester from step 3 was then hydrolyzed according to step 2 Example 117 to yield the title acid. m/z (M-1)521.3

Example 124

sodium 3-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-3-oxopropanoic acid

Step 1 The intermediate from example 117, step 1 was acylated with methyl malonyl chloride according to the procedure for step 1 of Example 117 in 82 % yield.
Step 2 The ester was hydrolyzed according to step 2 for Example 123 to yield the title compound. m/z (M-1)507.2

Example 125

2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-2-oxoacetic acid

Step 1 The intermediate from example 117, step 1 was acylated with methyl oxalyl chloride according to the procedure for step 1 of Example 117 in 67 % yield.

Step 2 The ester was hydrolyzed according to step 2 for Example 117 to yield the title compound. m/z (M-1)493.2

Example 126

2-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]cyclopropanecarboxylic acid

Step 1: This intermediate compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and ethyl 2-formyl-1-cyclopropanecarboxylate according to the procedure in Example 117 Step 1 in 53% yield.

Step 2: The ester was hydrolyzed according to step 2 for Example 117 to yield the title compound in 93 % yield. m/z (M-1)1414.2

Example 127

2-[(1-benzhydryl-6-chloro-5-fluoro-1H-indol-3-yl)methyl]cyclopropanecarboxylic acid

Step 1: 6-chloro-5-flouroindole was N-alkylated with benzhydryl bromide according to the procedure in Example 69 step 2 to yield the target intermediate.

Step 2: The product from step 1 was C3 acylated with ethyl 2-formyl-1-cyclopropanecarboxylate according to the procedure in Example 117 Step 1 in 53% yield.

Step 3: The ester was hydrolyzed according to step 2 for Example 117 to yield the title compound in 73 % yield. m/z (M-1)432.2

Example128

2-[(1-benzhydryl-5,6-dichloro-1H-indol-3-yl)methyl]cyclopropanecarboxylic acid

Step 1: 5,6-dichloroindole was n alkylated with benzhydryl bromide according to the procedure in Example 69 step 2 to yield the target intermediate in 70% yield.

Step 2: The intermediate from step 1 was C3 acylated with ethyl 2-formyl-1-cyclopropanecarboxylate according to the procedure in Example 117 Step 1 in 62% yield.

Step 3: The ester was hydrolyzed according to step 2 for Example 117 to yield the title compound in 73 % yield. m/z (M-1)448.2

Example 129

2-({1-[bis(4-hydroxyphenyl)methyl]-6-chloro-1H-indol-3-yl}methyl)cyclopropanecarboxylic acid

Step 1: 6-chloroindole was C3 alkylated with ethyl 2-formyl-1-cyclopropanecarboxylate according to the procedure in Example 117 Step 1.

Step 2: The intermediate ffrom step 1 (2.0 eq.) was dissolved in THF (0.5 M) and cooled to –40°C and then triethylamine (2.0 eq) was added followed by methanesulfonyl chloride (2.0 eq). The reaction was stirred at this temperature until TLC analysis indicated no more starting alcohol, and then it was cannulated directly into a mixture of the c3 alkylated indole from step 1 (1.0 eq) in DMF (1.0 M) at –20°C that had been stirred for 30 minutes at room temperature with sodium hydride (4.0 eq of a 60% dispersion). The resulting mixture was warmed to room temperature overnight and quenched when the reaction was deemed complete by the addition of saturated ammonium chloride, diluted with ethyl acetate and washed with saturated ammonium chloride, saturated sodium bicarbonate and water (2X), dried, concentrated and purified by column chromatography.

Step 3: The intermediate from step 2 was dissolved in THF (1.0M) and treated with a solution of tetrabutylammonium flouride (2.5 eq) and stirred at room temperature until TLC analysis indicates that both silyl ethers had been cleaved. The reaction was then poured into saturated ammonium chloride and extracted with ethyl acetate (3X), the combined organic washed were washed with water, brine, dried and concentrated and purified by column chromatography to yield the intermediate in 73 % yield.

Step 4: The ester from step 3 was hydrolyzed according to step 2 for Example 123 to yield the title compound in 92% yield. m/z (M-1)447.12

Example 130

'4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-hydroxybenzoic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and 4-hydroxy-2-methoxybenzaldehyde according to the procedure in Example 117 Step 1.

Step 2: The ester was hydrolyzed according to step 2 for Example 117 to yield the title compound

Example 131

'4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-(3-hydroxypropoxy)benzoic acid

Step 1: The intermediate from Example 130, step 1, was dissolved in DMF (1.0M), solid potassium carbonate (3 eq) followed by 2-(3-bromopropoxy)tetrahydro-2H-pyran (1.5 eq) was added and the reaction was left to stir for 24 hours at room temperature. The workup consisted

of diluting with half saturated ammonium chloride and ethyl acetate, extracting aqueous layer with ethyl acetate (2X), washing the organic layer with water (2X), drying, concentration followed by purification via column chromatography.

Step 2: The intermediate from step 1 was dissolved in THF (1.0M), treated with glacial acetic acid (2.0 eq) and heated at 45°C for 24 hours, at which time the reaction was partitioned between saturated sodium bicarbonate and ethyl acetate, the combined organic layers where washed with water (2X), dried, concentrated and purified by column chromatography to yield 88% of the desired compound.

Step 3: The ester was hydrolyzed according to step 2 for Example 123 to yield the title compound. m/z (M-1)524.3

Example 132

'4-({1-[(4-aminophenyl)(phenyl)methyl]-6-chloro-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1:This compound was prepared from 6 chloroindole and methyl 2-(4-formyl-2-methoxyphenoxy)acetate according to the procedure in Example 117 Step 1 in 61% yield.

Step 2: The intermediate from step 1 was N-alkylated according to the procedure for Example 129, step 2, with tert-butyl N-{4-[hydroxy(phenyl)methyl]phenyl}carbamate.

Step 3: The nitrogen protection was removed by heating the compound to 180°C to yield 45% of the desired amino ester.

Step 4: The intermediate from step 3 was hydrolyzed following step 2 for Example 117 to yield the title compound in 78% yield. m/z (M-1)495.2

Example 133

'4-({6-chloro-1-[(4-methoxyphenyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1: The intermediate from Example 132, step 1, (1.0 eq) was dissolved in DMF (1.0M), cooled to 0°C, and treated with sodium hydride (1.5 eq) and stirred for 30 minutes to affect deprotonation. The 1-[bromo(phenyl)methyl]-4-methoxybenzene (1.5 eq), as a solution in DMF (2.0M), was added to the anion and the reaction was warmed to room temperature, when the reaction was deemed complete by TLC analysis it was partitioned between ethyl acetate and half saturated ammonium chloride, extracting the aqueous layer with ethyl acetate (2X), washing the organic layer with water (2X), drying, concentration followed by purification via column chromatography yielded the desired intermediate.

Step 2: The intermediate from step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound. m/z (M-1)510.2

Example 134

'4-({1-[bis(4-methoxyphenyl)methyl]-6-chloro-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1: The intermediate from Example 132 was N-alkylated with 1-[bromo(4-methoxyphenyl)methyl]-4-methoxybenzene according to the procedure described in Example 133, step 1, to yield the desired intermediate.

Step 2: The intermediate from step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound. m/z (M-1)540.3

Example 135

'4-({6-chloro-1-[(2-morpholinophenyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1: The intermediate from Example 132 was N-alkylated according to the procedure for Example 129, step 2, with the appropriate electrophile.

Step 2: The intermediate form step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound.

Example 136

4-({6-chloro-1-[(2,4-dimethoxy-5-pyrimidinyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid

Step 1: The intermediate from Example 132 was N-alkylated according to the procedure for Example 129, step 2, with the appropriate electrophile to yield the desired intermediate in 16% yield.

Step 2: The intermediate from step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound. m/z (M-1)542.3

Example 137

'4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid

Step 1:This compound was prepared from the 1-benzhydryl-6-chloro-1H-indole and the appropriate aldehyde according to the procedure in Example 117 Step 1.

Step 2: The intermediate from step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound. m/z (M-1)481.14

Example 138

2-({4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxybenzoyl}amino)acetic acid

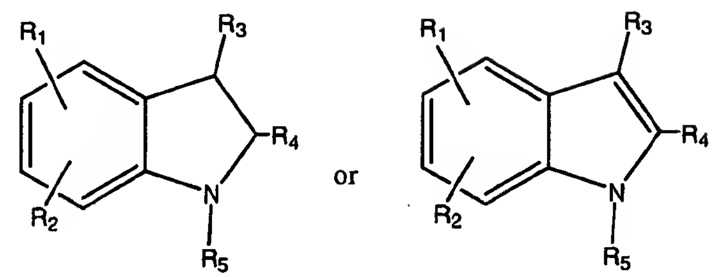
Step 1: The intermediate from Example 137, step 2, treated with glycine ethyl ester according to the procedure in Example 76 to yield the desired ester.

Step 2: The intermediate from step 1 was hydrolyzed following step 2 for Example 117 to yield the title compound. m/z (M-1)537.2

All patents and literature references cited herein are incorporated as if fully set forth herein.

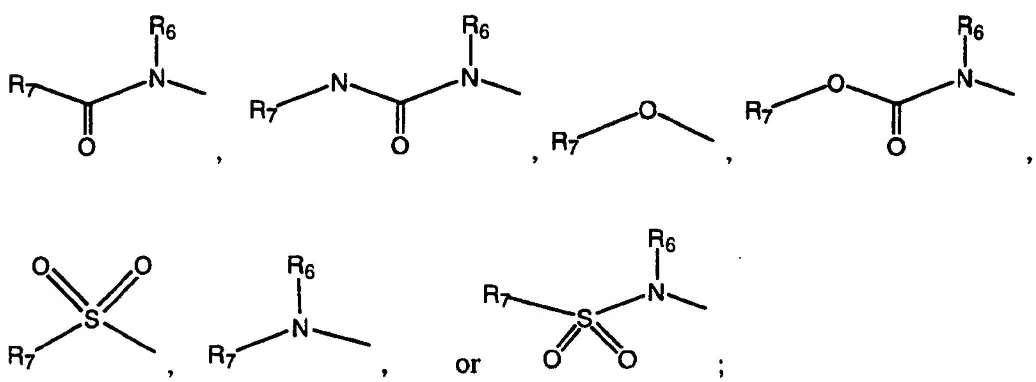
What is claimed is:

1) A compound of the formulae:



wherein:

R_1 is selected from H, halogen, $-CF_3$, -OH, $-C_1-C_{10}$ alkyl, $-S-C_1-C_{10}$ alkyl, C_1-C_{10} alkoxy, -CN, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, -S-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

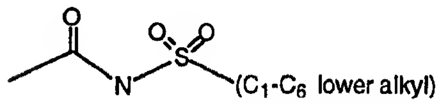


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, -CN, $-CF_3$, or -OH;

R_7 is selected from -OH, $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH-(C_1-C_6$ alkyl), $-N-(C_1-C_6$ alkyl$)_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl and thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, -CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_{10} alkyl, C_1-C_{10} alkoxy-CHO, -CN, -NO_2, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_n$-tetrazole,



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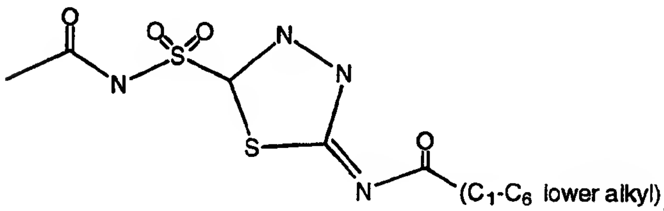

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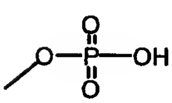

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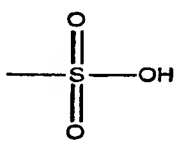
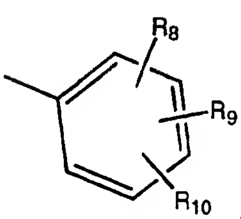


or a moiety selected from the formulae $-L^1$-M^1;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n$-, -S-, -O-, -C(O)-, $-(CH_2)_n$-C(O)-, $-(CH_2)_n$-C(O)-$(CH_2)_n$-, $-(CH_2)_n$-O-$(CH_2)_n$-,$-(CH_2)_n$-S-$(CH_2)_n$-, -C(Z)-N(R_6)-, -C(Z)-N(R_6)-$(CH_2)_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-$(CH_2)_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-$(CH_2)_n$-;

M^1 is selected from the group of -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, tetrazole,



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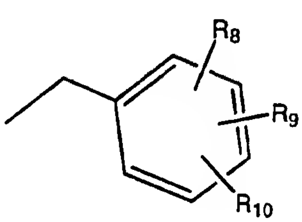

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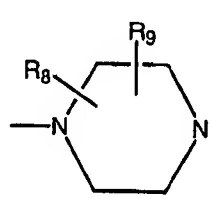

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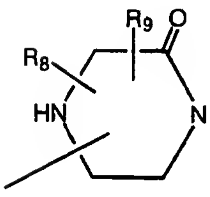
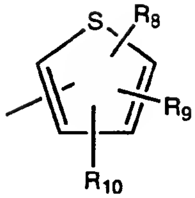
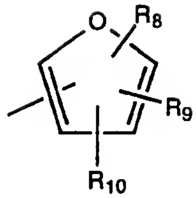
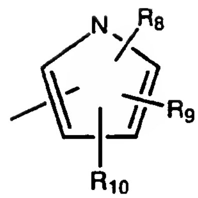
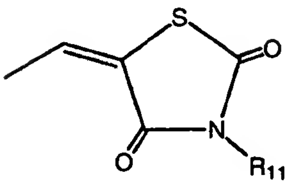
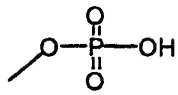
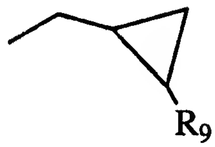
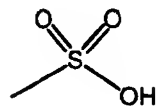
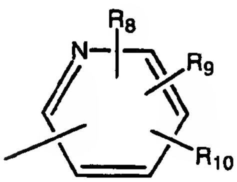
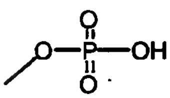
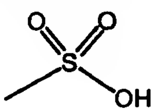
, , , ,

, , , 

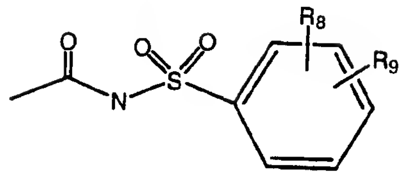
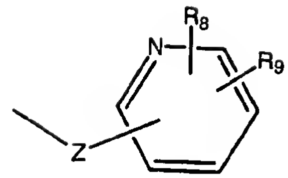
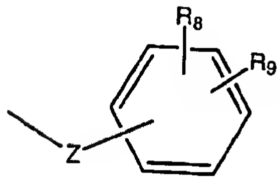
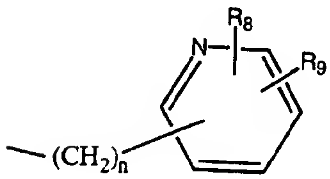
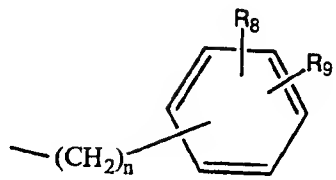
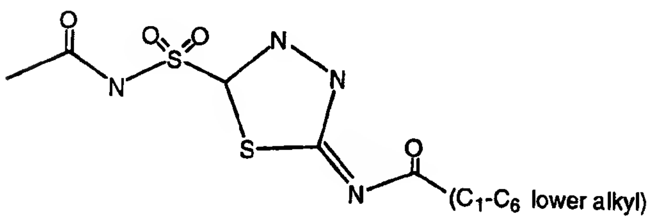
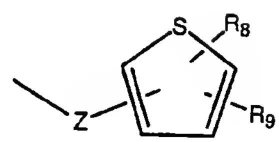
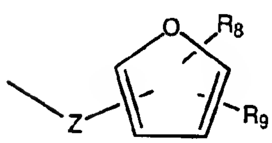
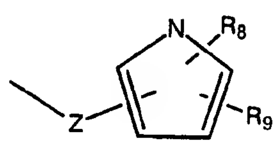
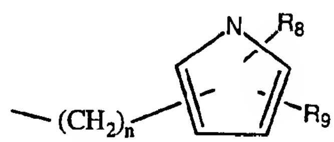
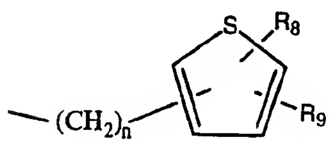
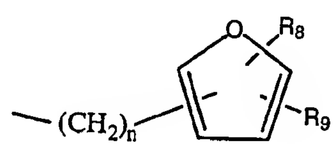
or ;

R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

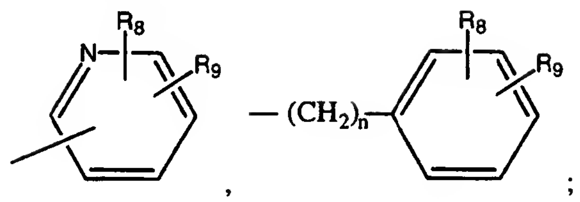
 ,or ;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -O-$(CH_2)_n$-COOH, -O-CH_2-C=C-COOH, -O-C=C-CH_2-COOH, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -N-C(O)-$(CH_2)_n$-COOH, -N-SO_2-$(CH_2)_n$-COOH, -C(O)-N-$(CH_2)_n$-COOH;

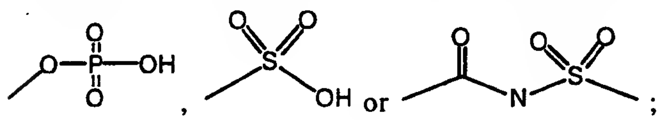
R_{10} is selected from the group of H, halogen, -CF_3, -OH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -O-(C_1-C_6 alkyl)-$(OH)_n$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -N-C(O)-N-(C_1-C_6 alkyl)-$(OH)_2$,

,
,
,
,
,
,
,
,

,
, or
;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, -CF_3, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH,



with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:



n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^2 is selected from the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

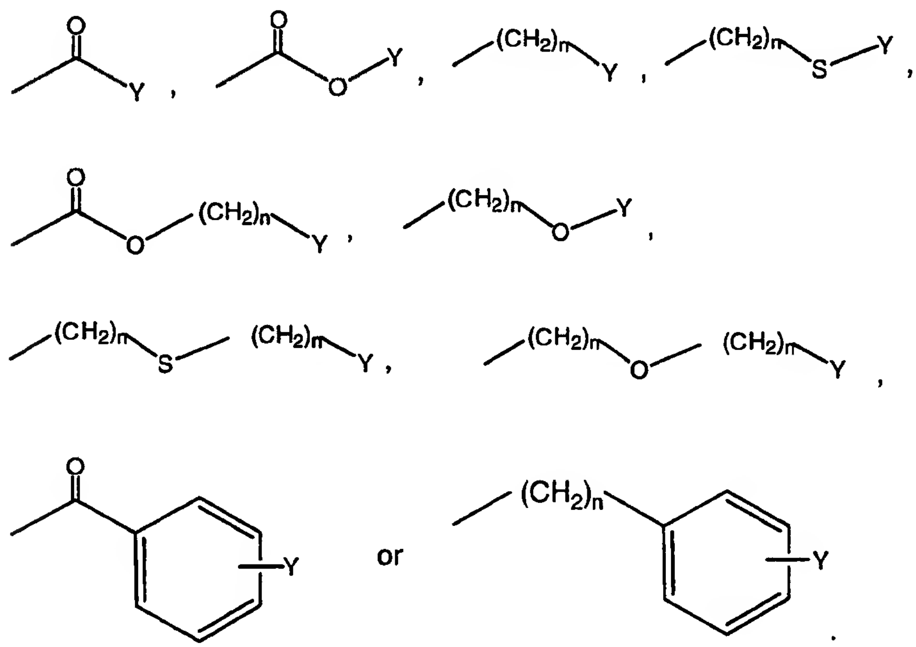
a) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

b) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to pyridine, pyrimidine, piperidine, piperazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

c) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, indole, indoline, napthalene, purine, or quinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, -$(CH_2)_n$-C_3-C_{10} cycloalkyl,
-$(CH_2)_n$-S-$(CH_2)_n$-C_3-C_{10} cycloalkyl, -$(CH_2)_n$-O-$(CH_2)_n$-C_3-C_{10} cycloalkyl, or the groups of:

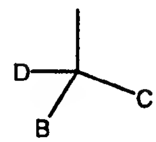
a) -$(CH_2)_n$-phenyl-O-phenyl, -$(CH_2)_n$-phenyl-CH_2-phenyl, -$(CH_2)_n$-O-phenyl-CH_2-phenyl, -$(CH_2)_n$-phenyl-(O-CH_2-phenyl)$_2$, -CH_2-phenyl-C(O)-benzothiazole or a moiety of the formulae:



;

wherein n is an integer from 0 to 3, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole and pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -CN, -NH_2, -NO_2 or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O; or

b) a moiety of the formulae $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-CF_3$ or $-(CH_2)_n-CF_3$;

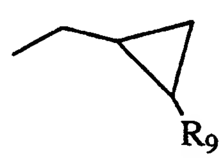
B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, preferably 1 to 2, substituents selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-N(C_1-C_6)_2$, $-NH(C_1-C_6)$, $-N-C(O)-(C_1-C_6)$, $-NO_2$, or by a 5- or 6-membered heterocyclic or heteroaromatic ring containing 1 or 2 heteroatoms selected from O, N or S; or a pharmaceutically acceptable salt thereof.

2. A compound of Claim 1 wherein R_1., R_4, and R_2 are hydrogen, or a pharmaceutically acceptable salt thereof.

3. A compound of Claim 2 further wherein R_1 is in the indole or indoline 5-position, or a pharmaceutically acceptable salt thereof.

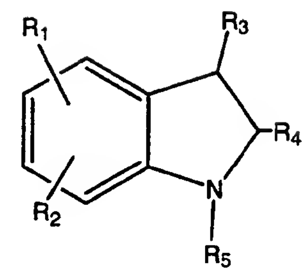
4. A compound of Claim 3 further wherein R_1 is a benzyloxy group, or a pharmaceutically acceptable salt thereof.

5. A compound of Claim 1 wherein R_3 is $-L^1-M^1$, M^1 is the moiety:

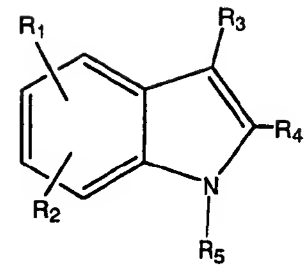


and L^1 and R_9 are as defined in Claim 1

6. A compound having the formulae:

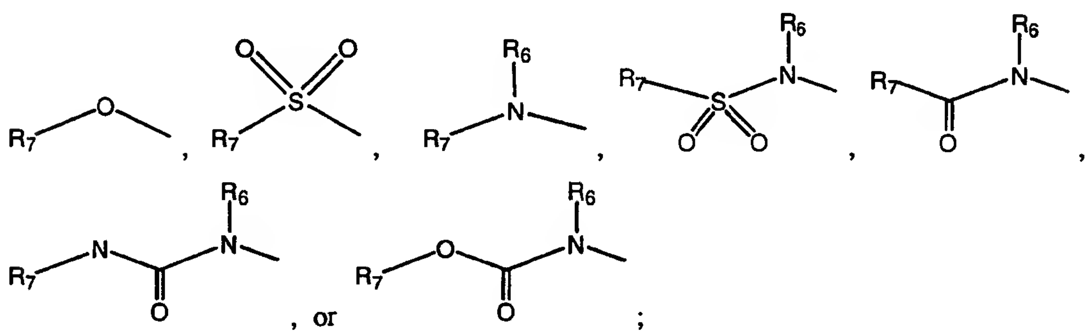


or



wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, CN, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

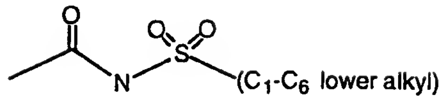


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl and thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



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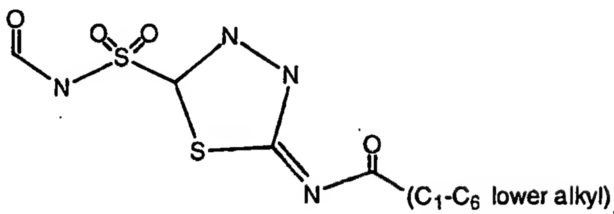

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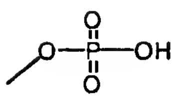

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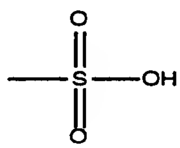
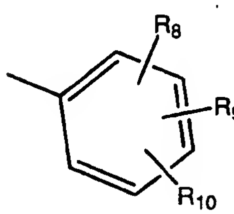


or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$,$-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^1 is selected from the group of -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,



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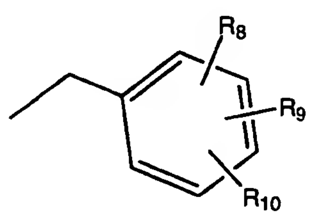

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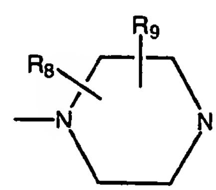

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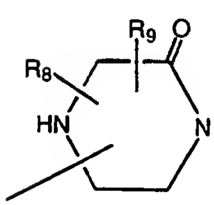

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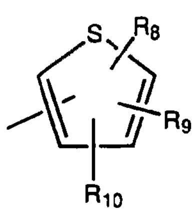

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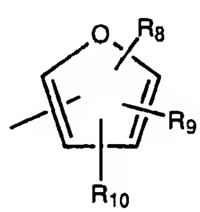

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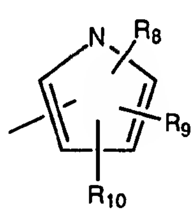

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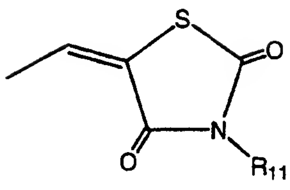
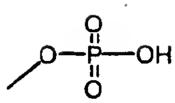
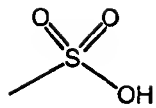
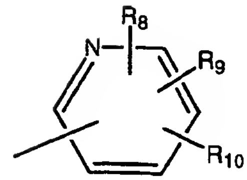
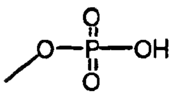
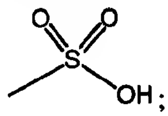
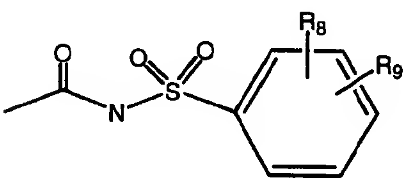
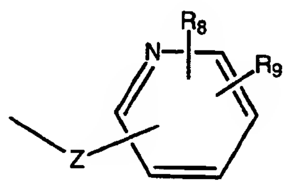
, ,  or 

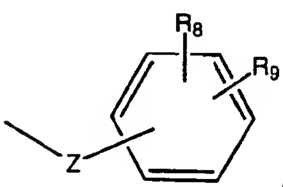
R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

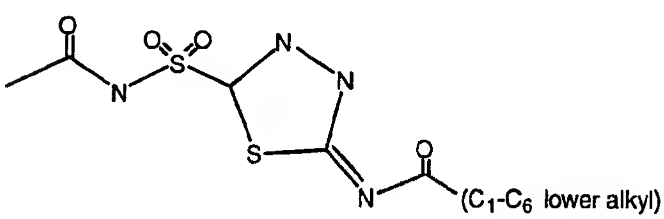
, or ;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$,

, ,

 or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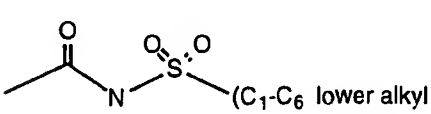
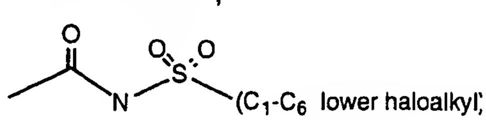
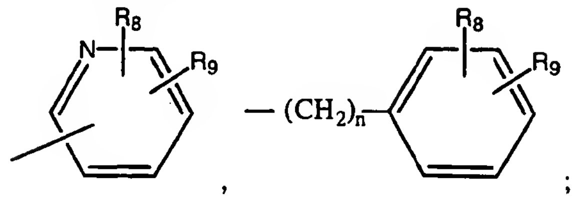
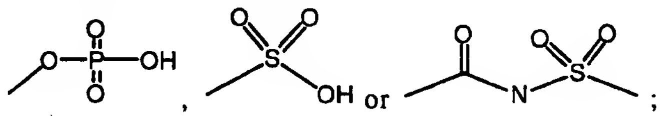

, 
;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, -CF_3, -COOH. -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH,



with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:



n is an integer from 0 to 3;

R_4 is selected from H, -CF_3, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, -C_1-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula -L^2-M^2:

L^2 indicates a linking or bridging group of the formulae -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-, or -$(CH_2)_n$-S-$(CH_2)_n$-;

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -NO_2, -NH_2, -CN, or -CF_3; or

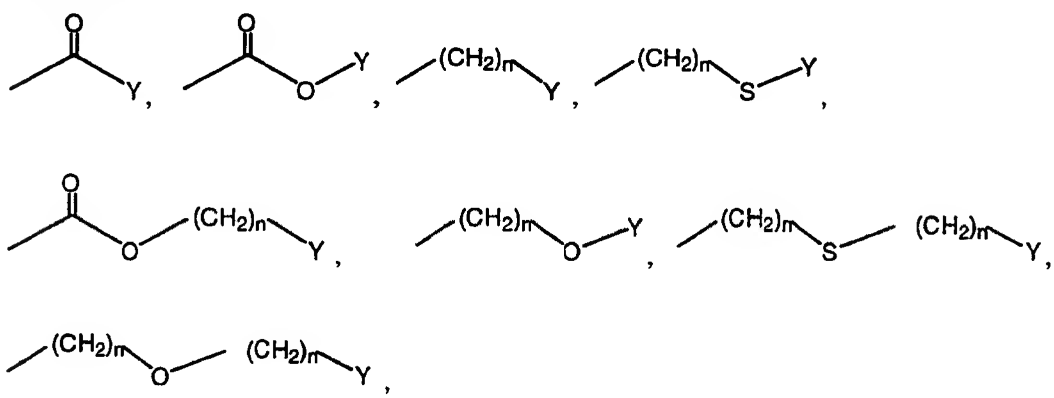
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -NO_2, -NH_2, -CN, or -CF_3; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH;

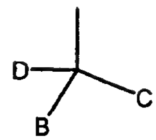
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, -$(CH_2)_n$-C_3-C_5 cycloalkyl, -$(CH_2)_n$-S-$(CH_2)_n$-C_3-C_5 cycloalkyl, -$(CH_2)_n$-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, or the groups of:

a) -$(CH_2)_n$-phenyl-O-phenyl, -$(CH_2)_n$-phenyl-CH_2-phenyl, -$(CH_2)_n$-O-phenyl-CH_2-phenyl, -$(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, -CH_2-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl benzothiazole or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NO_2, -NH_2 or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O; or

b) a moiety of the formulae -$(CH_2)_n$-A, -$(CH_2)_n$-S-A, or -$(CH_2)_n$-O-A, wherein A is the moiety:



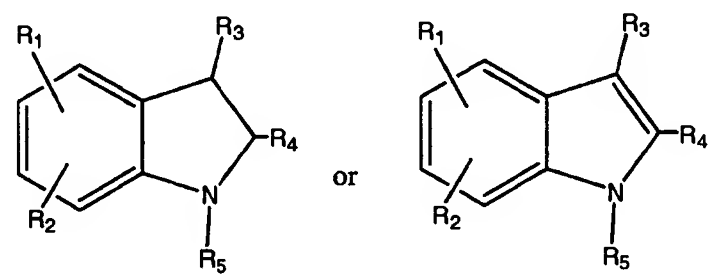
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n-CF_3$ or $-CF_3$;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$ or $-NO_2$;
or a pharmaceutically acceptable salt thereof.

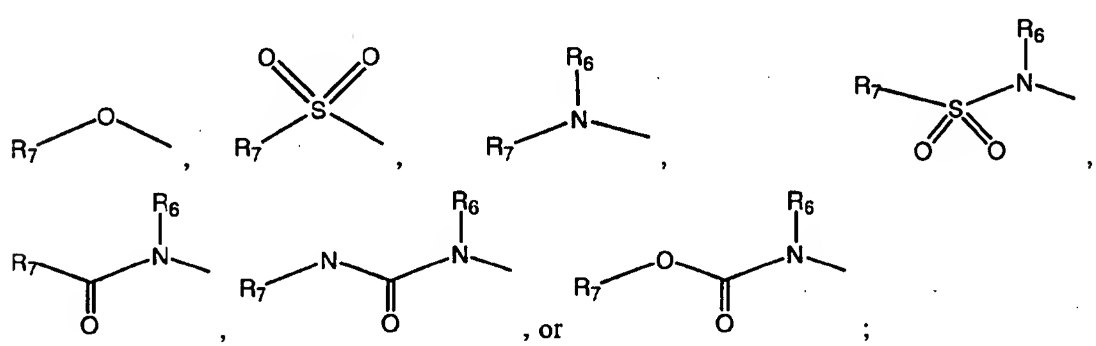
7. A compound of Claim 5 wherein the R_1 substitution is at the indole or indoline ring's 5-position, or a pharmaceutically acceptable salt thereof.

8. A compound having the formulae:



wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

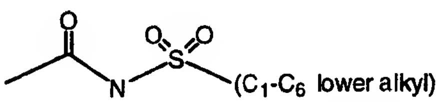


R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-CF_3$, or -OH;

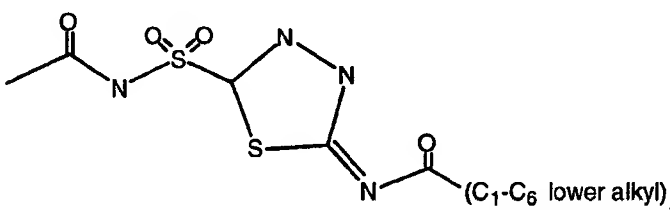
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl or thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

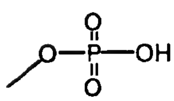
R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,



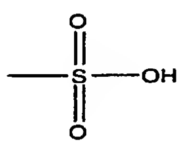
or



, or



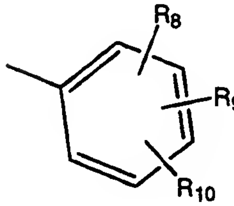
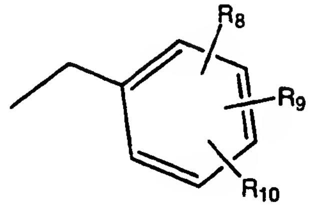
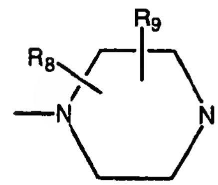
, or

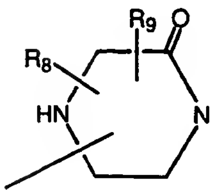
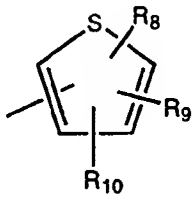
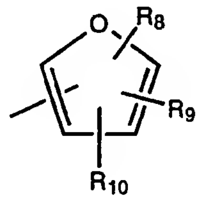
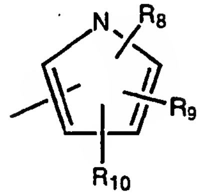


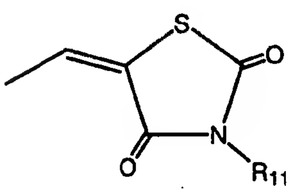
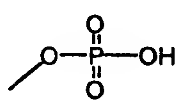
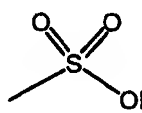
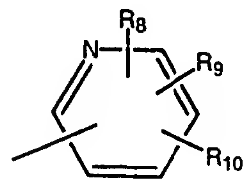
or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-, -$(CH_2)_n$-S-$(CH_2)_n$-, -C(Z)-N(R_6)-, -C(Z)-N(R_6)-$(CH_2)_n$-, -C(O)-C(Z)-N(R_6)-, -C(O)-C(Z)-N(R_6)-$(CH_2)_n$-, -C(Z)-NH-SO_2-, or -C(Z)-NH-SO_2-$(CH_2)_n$-;

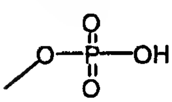
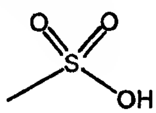
M^1 is selected from the group of -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

, , ,

, , , ,

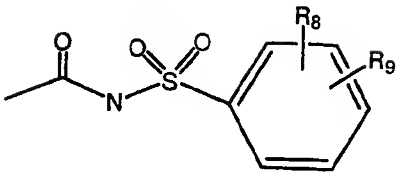
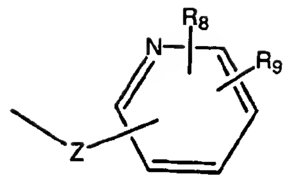
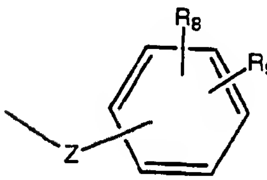
, ,  or 

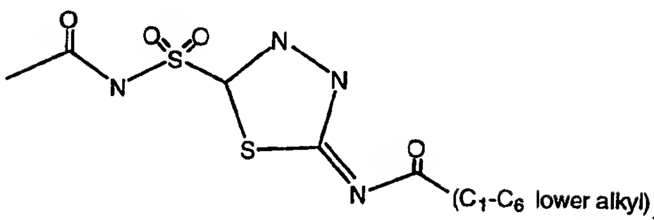
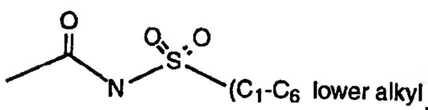
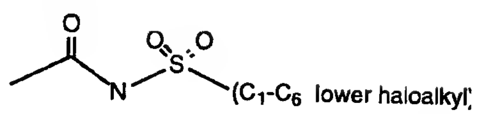
R_8, in each appearance, is independently selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, tetrazole,

,or ;

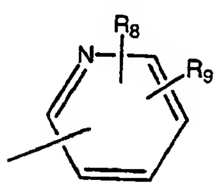
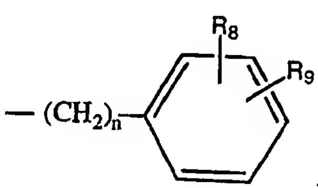
R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,

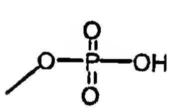
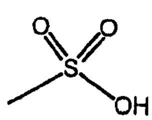
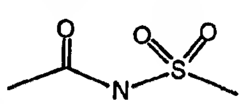
,
,
 or

,
, or ;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,

, ;

with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:

,  or ;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2$-M^2:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^2 is selected from:

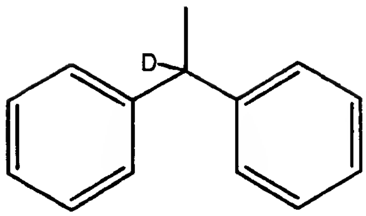
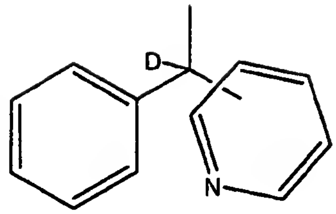
a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

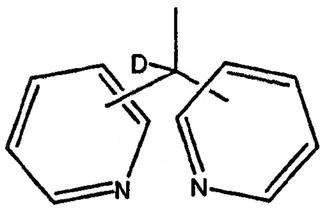
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

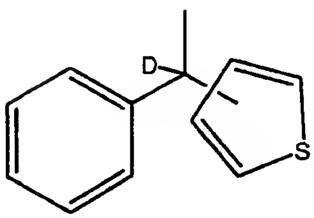
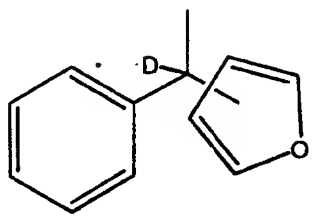
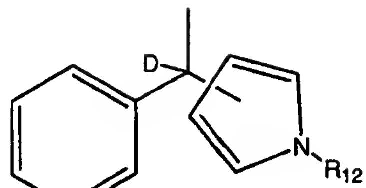
c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

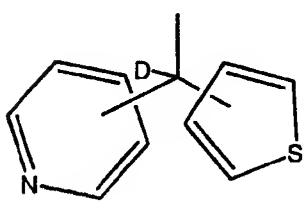
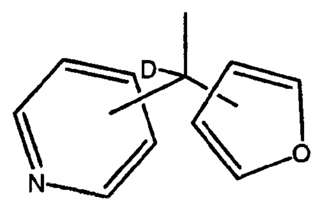
d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH;

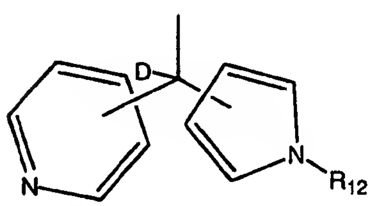
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n-C_3-C_5$ cycloalkyl or $--(CH_2)_n-A$, $-(CH_2)_n-S-A$, or $-(CH_2)_n-O-A$ wherein A is selected from :

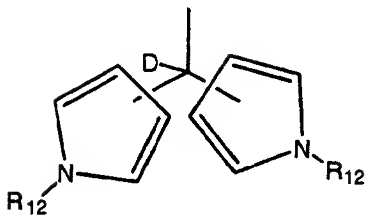
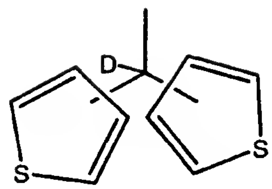
 ,  ,

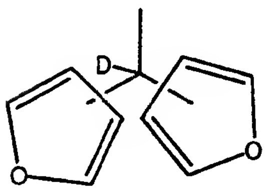
 ,

 ,  ,  ,

 ,  ,

 ,

 ,  , or

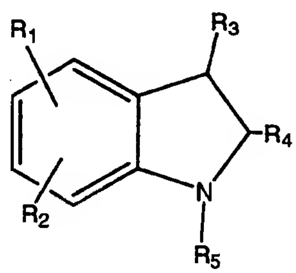
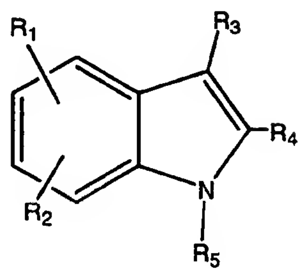
 ;

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

R_{12} is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

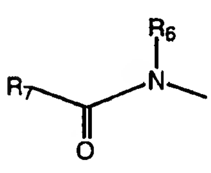
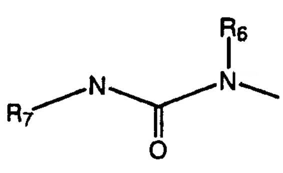
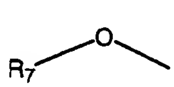
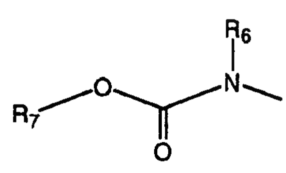
or a pharmaceutically acceptable salt thereof.

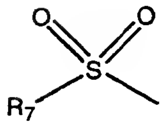
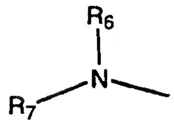
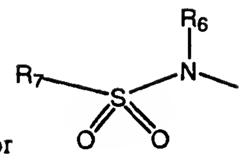
9. A compound of the formulae:

 or 

wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

 ,  ,  ,  ,

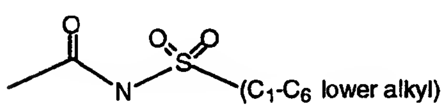
, , or ;

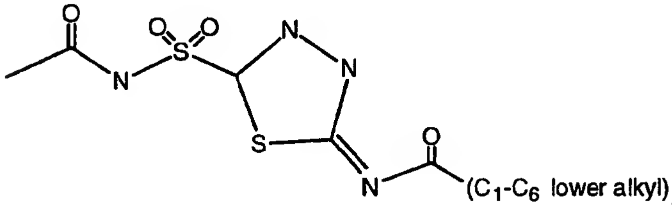
R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

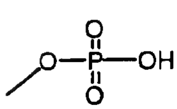
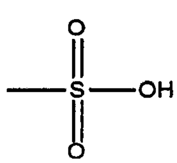
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, pyrazolyl, thiazolyl, -O-phenyl, benzyl, or -O-benzyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$-tetrazole,

 or

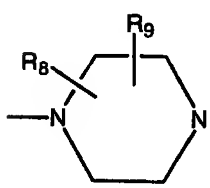
, or

, or 

or a moiety selected from the formulae -L^1-M^1 or L^2M^2;

L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$,$-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^1 is selected from the group of -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,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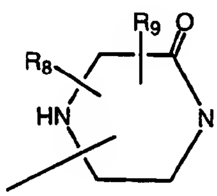
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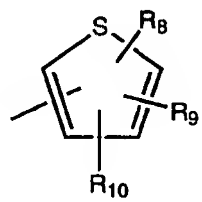
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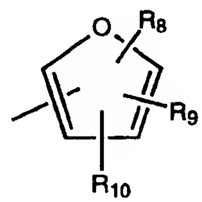
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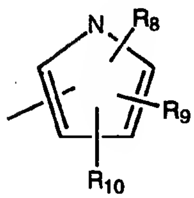
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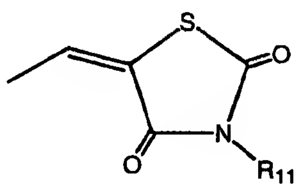
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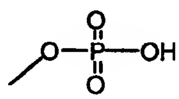
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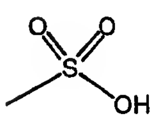
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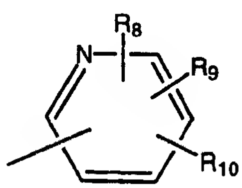
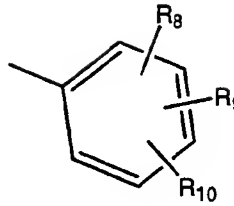


L^2 is a bridging or linking moiety selected from a chemical bond -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, $-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^2 is the moiety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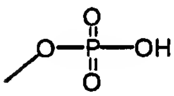
R_8, in each appearance, is independently selected from H, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, tetrazole,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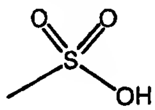
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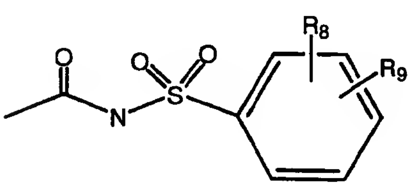
R_9 is selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$;

R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,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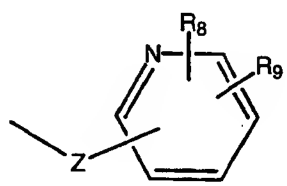
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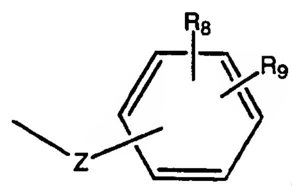
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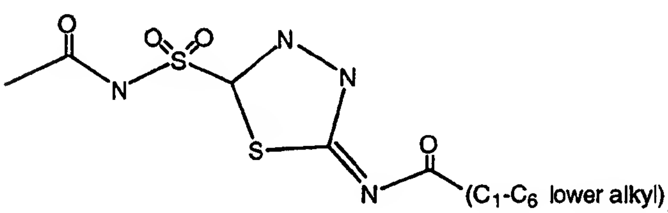
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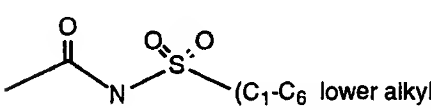
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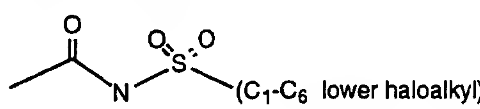
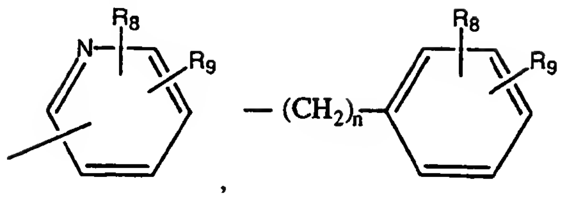
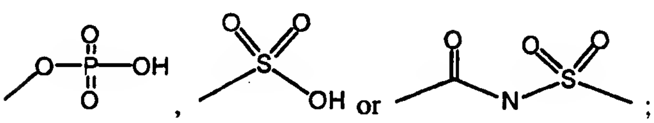

;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH,



with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, L^2, M^2, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:



n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, $-C_1$-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^3-M^3$:

L^3 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^3 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

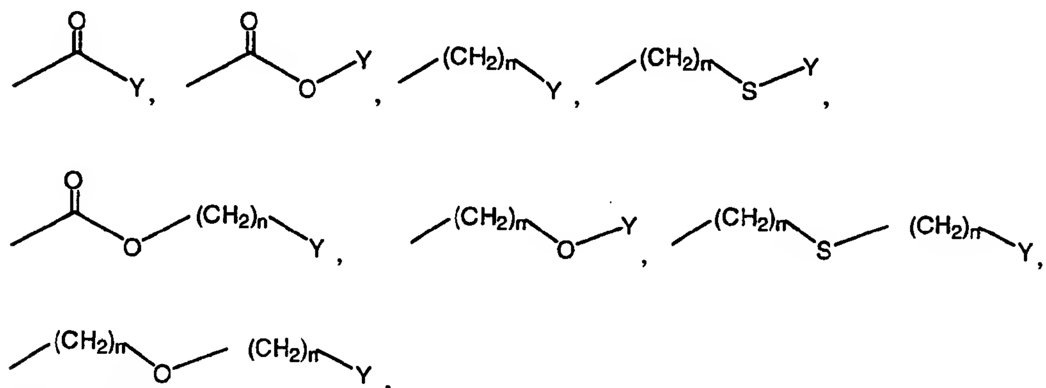
c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine,

piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -NO_2, -NH_2, -CN, -CF_3 or -OH;

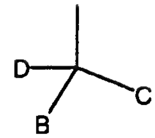
R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, -$(CH_2)_n$-C_3-C_5 cycloalkyl, -$(CH_2)_n$-S-$(CH_2)_n$-C_3-C_5 cycloalkyl, -$(CH_2)_n$-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, or the groups of:

a) -$(CH_2)_n$-phenyl-O-phenyl, -$(CH_2)_n$-phenyl-CH_2-phenyl, -$(CH_2)_n$-O-phenyl-CH_2-phenyl, -$(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, -CH_2-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole, or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH_2, -NO_2 or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O; or

b) a moiety of the formulae -$(CH_2)_n$-A, -$(CH_2)_n$-S-A, or -$(CH_2)_n$-O-A, wherein A is the moiety:



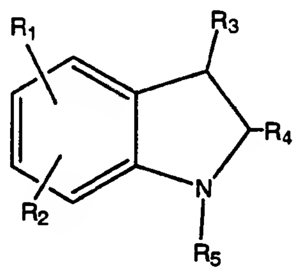
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-CF_3$ or $-(CH_2)_n$-CF_3;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$ or $-NO_2$;

or a pharmaceutically acceptable salt thereof.

10. A compound of the formulae:



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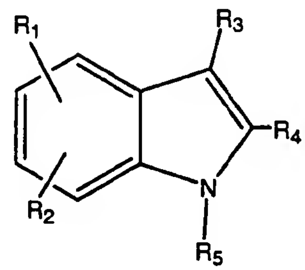
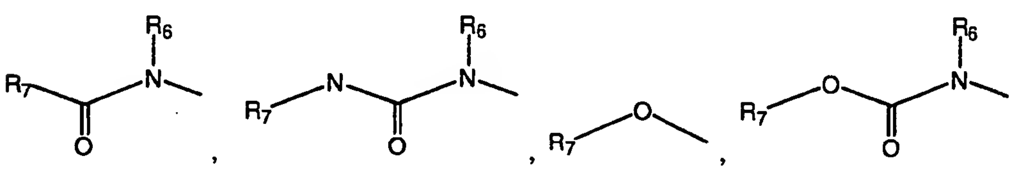
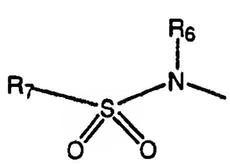


wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:



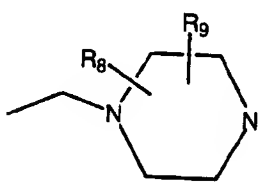
or  ;

R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl or thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, -$(CH_2)_n$-C(O)-COOH, -$(CH_2)_n$-COOH, -CH=CH-COOH, -$(CH_2)_n$C(O)NS(O)(O)(C_1-C_6 lower alkyl), -$(CH_2)_N$C(O)NS(O)(O)(C_1-C_6 lower haloalkyl),



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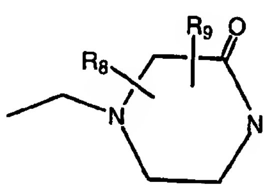

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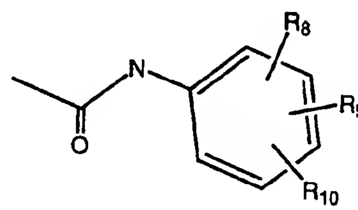

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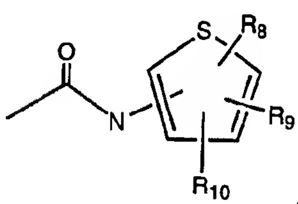

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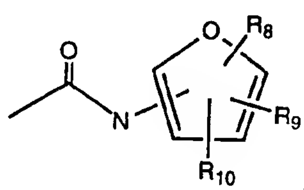

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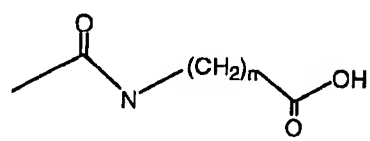

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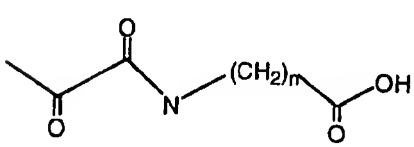

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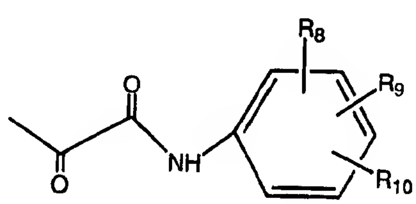

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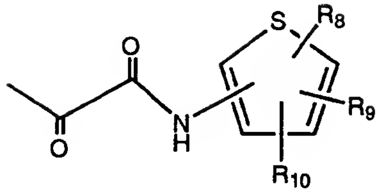
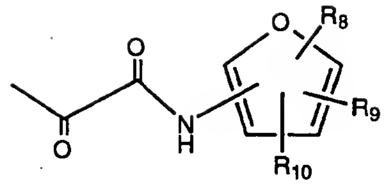
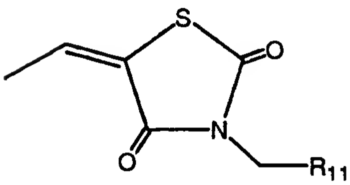
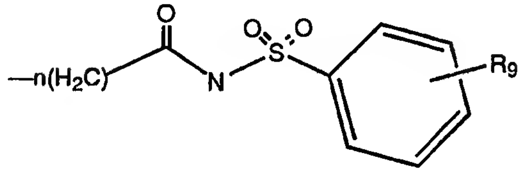
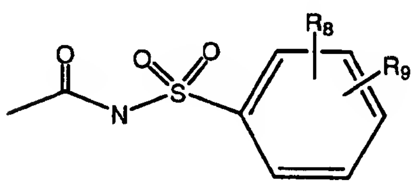
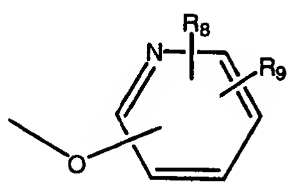
, , or

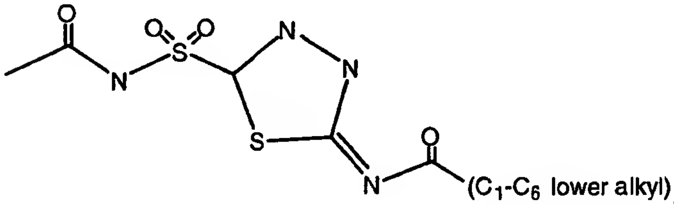
, ;

R_8 is selected from H, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH;

R_9 is selected from H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$;

R_{10} is selected from the group of H, halogen, -CF_3, -OH, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, -C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$,

, , or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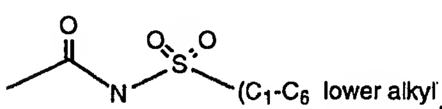
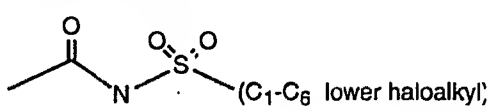
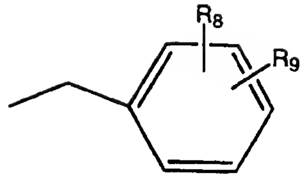

, 
;

R_{11} is selected from H, C_1-C_6 lower alkyl, -CF_3, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH, or



;

n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, -C_1-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula $-L^2-M^2$:

L^2 indicates a linking or bridging group of the formulae $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, or $-(CH_2)_n-S-(CH_2)_n-$;

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

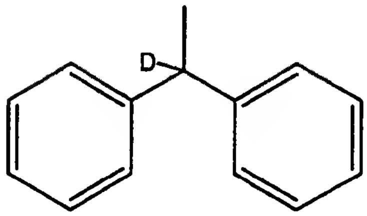
b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3

substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl or $--(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A wherein A is selected from :



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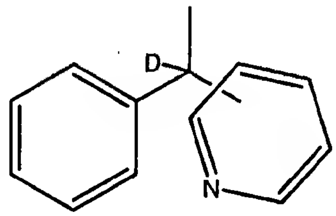

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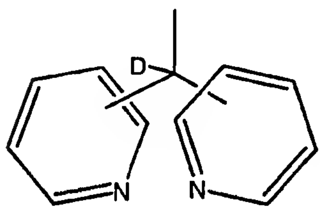

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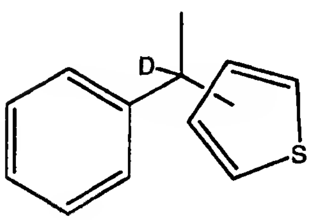

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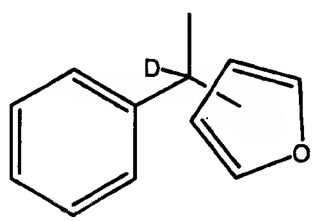

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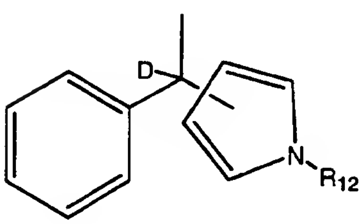

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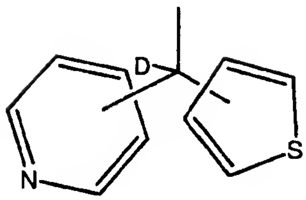
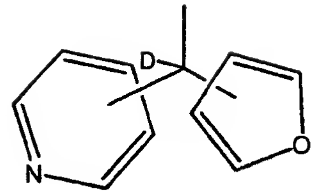
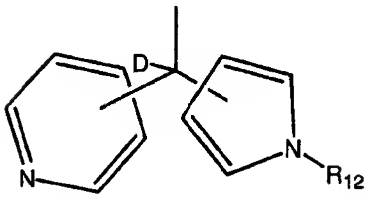
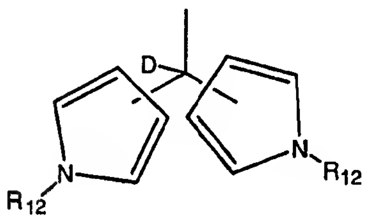
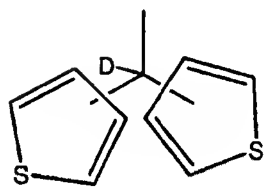
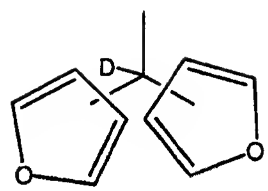
 ,  ,

 ,

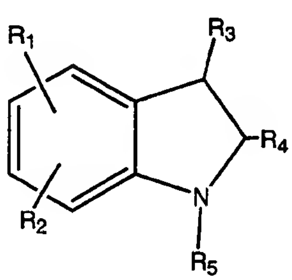
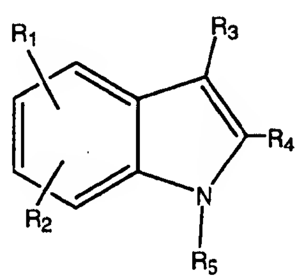
 ,  , or  ;

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or -CF_3;

R_{12} is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or -CF_3;

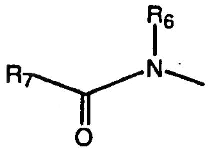
or a pharmaceutically acceptable salt thereof.

11. A compound of the formulae:

 or 

wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae: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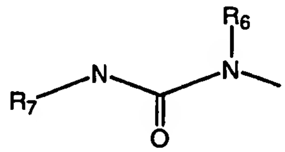
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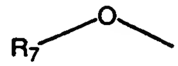
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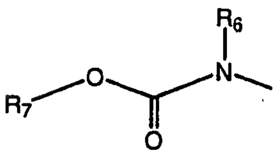
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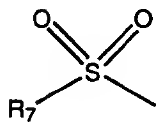
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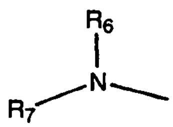
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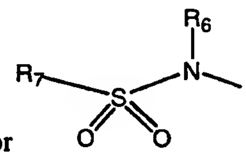
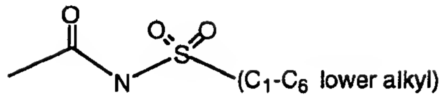

;

R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, pyrazolyl, thiazolyl, -O-phenyl, benzyl or -O-benzyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, $-CF_3$, or -OH;

R_2 is selected from H, halogen, -CN, -CHO, $-CF_3$, -OH, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, -CN, $-NO_2$, $-NH_2$, -NH-C_1-C_6 alkyl, -N(C_1-C_6 alkyl)$_2$, -N-SO_2-C_1-C_6 alkyl, or -SO_2-C_1-C_6 alkyl;

R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_n$-tetrazole,



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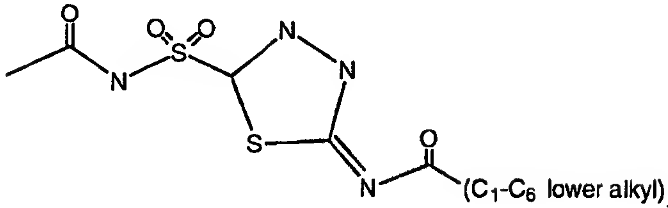

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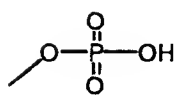

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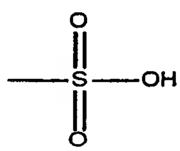
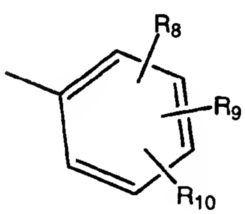


or a moiety selected from the formulae $-L^1-M^1$;

wherein L^1 is a bridging or linking moiety selected from a chemical bond, $-(CH_2)_n-$, -S-, -O-, -C(O)-, $-(CH_2)_n-C(O)-$, $-(CH_2)_n-C(O)-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_n-$, $-(CH_2)_n-S-(CH_2)_n-$, $-C(Z)-N(R_6)-$, $-C(Z)-N(R_6)-(CH_2)_n-$, $-C(O)-C(Z)-N(R_6)-$, $-C(O)-C(Z)-N(R_6)-(CH_2)_n-$, $-C(Z)-NH-SO_2-$, or $-C(Z)-NH-SO_2-(CH_2)_n-$;

M^1 is selected from the group of -COOH, $-(CH_2)_n-COOH$, $-(CH_2)_n-C(O)-COOH$, tetrazole,



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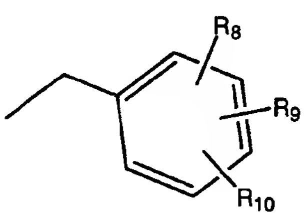

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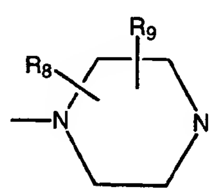

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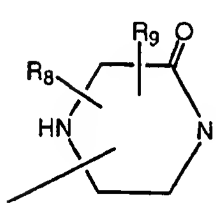

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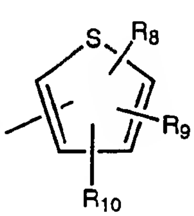

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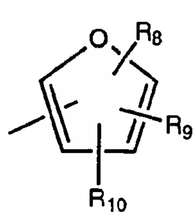

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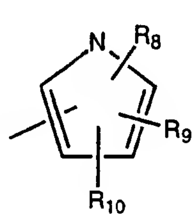

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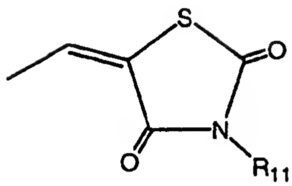
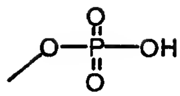
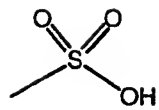
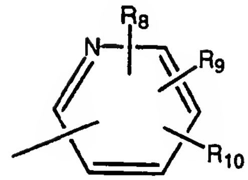
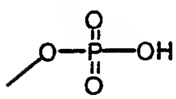
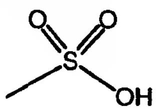
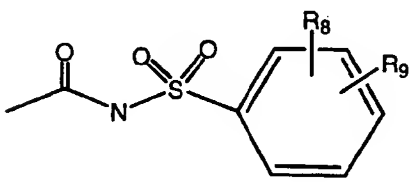
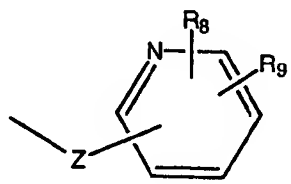
, ,  or 

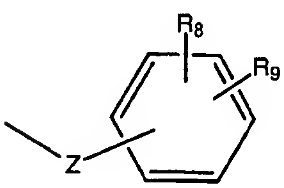
R_8, in each appearance, is independently selected from H, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, tetrazole,

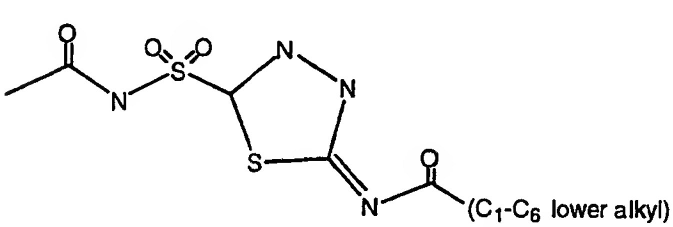
,or ;

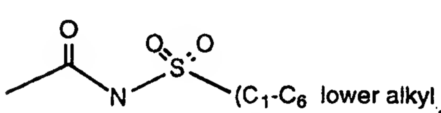
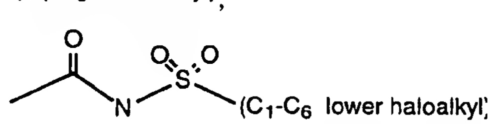
R_9 is selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$;

R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl$)_2$,

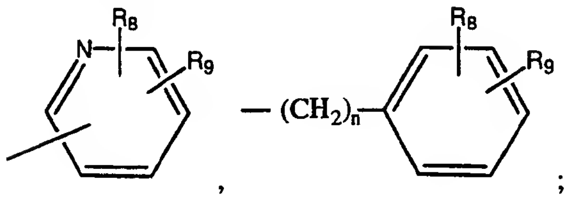
, ,

 or

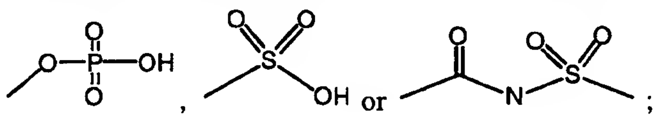
,

, ;

R_{11} is selected from H, C_1-C_6 lower alkyl, C_1-C_6 cycloalkyl, -CF_3, -COOH, -$(CH_2)_n$-COOH, -$(CH_2)_n$-C(O)-COOH,



with a proviso that the complete moiety at the indole or indoline 3-position created by any combination of R_3, L^1, M^1, R_8, R_9, R_{10}, and/or R_{11} shall contain at least one acidic moiety selected from or containing a carboxylic acid, a tetrazole, or a moiety of the formulae:



n is an integer from 0 to 3;

R_4 is selected from H, -CF_3, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, -C_1-C_6 alkyl-C_3-C_{10} cycloalkyl, -CHO, halogen, or a moiety of the formula -L^2-M^2:

L^2 indicates a linking or bridging group of the formulae -$(CH_2)_n$-, -S-, -O-, -C(O)-, -$(CH_2)_n$-C(O)-, -$(CH_2)_n$-C(O)-$(CH_2)_n$-, -$(CH_2)_n$-O-$(CH_2)_n$-, or -$(CH_2)_n$-S-$(CH_2)_n$-, -C(O)C(O)X;
where X is O or N,

M^2 is selected from:

a) the group of C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, C_3-C_{10} cycloalkyl, phenyl or benzyl, the cycloalkyl, phenyl or benzyl rings being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -NO_2, -NH_2, -CN, or -CF_3; or

b) a five-membered heterocyclic ring containing one or two ring heteroatoms selected from N, S or O including, but not limited to, furan, pyrrole, thiophene, imidazole, pyrazole, pyrrolidine, pyrazole, or tetrazole, the five-membered heterocyclic ring being

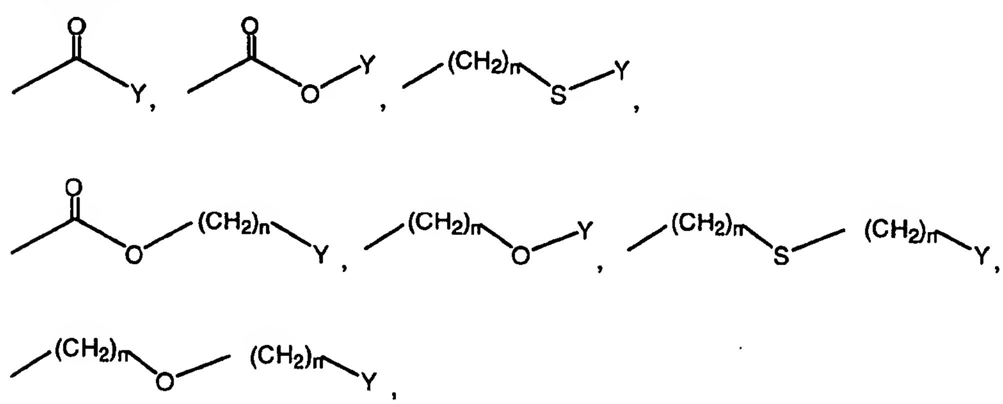
optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, $-NO_2$, $-NH_2$, -CN, or $-CF_3$; or

c) a six-membered heterocyclic ring containing one, two or three ring heteroatoms selected from N, S or O including, but not limited to, pyridine, pyrazine, pyrimidine, piperidine, piperazine, thiazine, or morpholine, the six-membered heterocyclic ring being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, $-CF_3$ or -OH; or

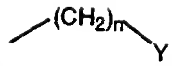
d) a bicyclic ring moiety containing from 8 to 10 ring atoms and optionally containing from 1 to 3 ring heteroatoms selected from N, S or O including, but not limited to benzofuran, chromene, indole, isoindole, indoline, isoindoline, napthalene, purine, quinoline or isoquinoline, the bicyclic ring moiety being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -CHO, $-NO_2$, $-NH_2$, -CN, -CF_3 or -OH;

R_5 is selected from $-(CH_2)_n$-S-$(CH_2)_n$-C_3-C_5 cycloalkyl, $-(CH_2)_n$-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, or the groups of:

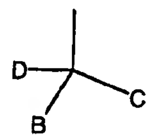
a) $-(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, $-(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, $-CH_2$-phenyl-C(O)-benzothiazole or a moiety of the formulae:



wherein n is an integer from 0 to 3, Y is C_3-C_5 cycloalkyl, phenyl, benzyl, napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, benzothiazole or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1$-C_6 alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O; or

b) a moiety of the formula  wherein n is an integer from 0 to 3, Y is napthyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl benzothiazole, or pyrimidinyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$ or a five membered heterocyclic ring containing one heteroatom selected from N, S, or O; or

c) a moiety of the formulae $-(CH_2)_n-A$, $-(CH_2)_n-S-A$, or $-(CH_2)_n-O-A$, wherein A is the moiety:



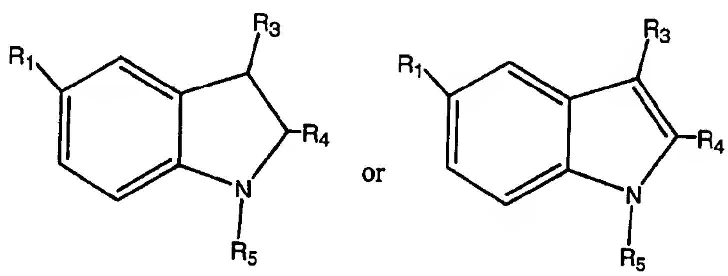
wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n-CF_3$ or $-CF_3$;

B and C are independently selected from phenyl, pyridinyl, pyrimidinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, substituents selected from H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NH_2$ or $-NO_2$;

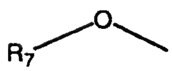
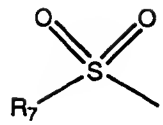
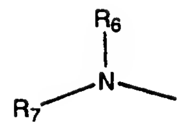
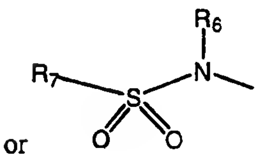
or a pharmaceutically acceptable salt thereof.

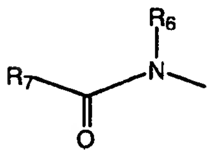
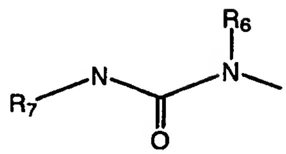
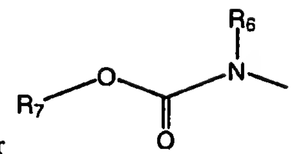
12. A compound of the formulae:



wherein:

R_1 is selected form H, halogen, $-CF_3$, -OH, $-C_1-C_6$ alkyl, C_1-C_6 alkoxy, $-NO_2$, $-NH_2$, phenyl, -O-phenyl, benzyl, -O-benzyl, -S-benzyl or a moiety of the formulae:

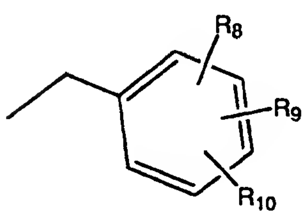
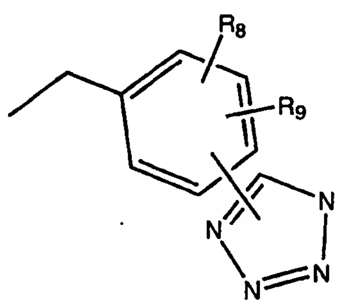
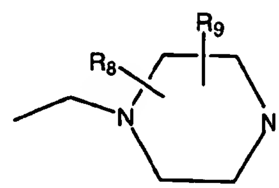
, , , or ,

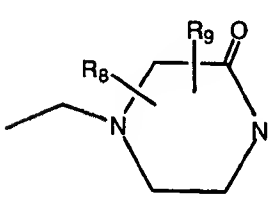
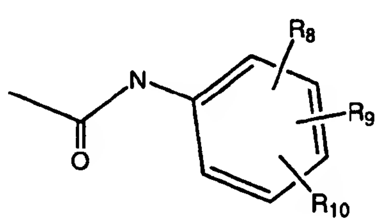
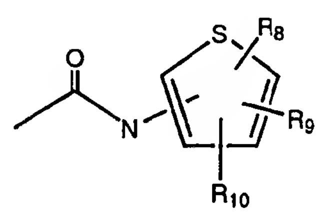
, , or  ;

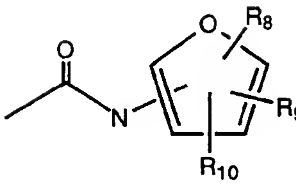
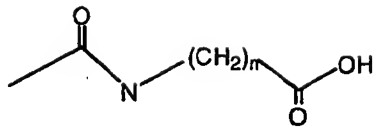
R_6 is selected from H, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -O-phenyl, benzyl, -O-benzyl, the phenyl and benzyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

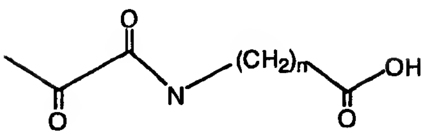
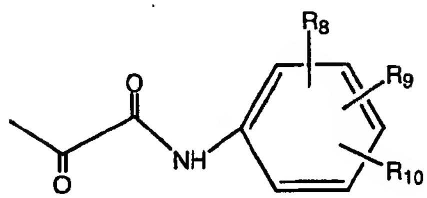
R_7 is selected from $-CF_3$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH-(C_1-C_6 alkyl), -N-(C_1-C_6 alkyl)$_2$, pyridinyl, thienyl, furyl, pyrrolyl, phenyl, -O-phenyl, benzyl, -O-benzyl, pyrazolyl or thiazolyl, the rings of these groups being optionally substituted by from 1 to 3 substituents selected from halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-NO_2$, $-CF_3$, or -OH;

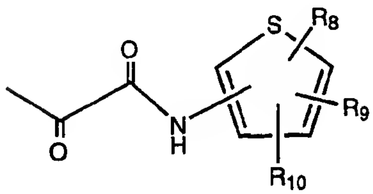
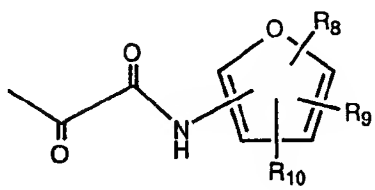
R_3 is selected from -COOH, -C(O)-COOH, $-(CH_2)_n$-C(O)-COOH, $-(CH_2)_n$-COOH, -CH=CH-COOH, $-(CH_2)_n$C(O)NS(O)(O)(C_1-C_6 lower alkyl), $-(CH_2)_N$C(O)NS(O)(O)(C_1-C_6 lower haloalkyl),

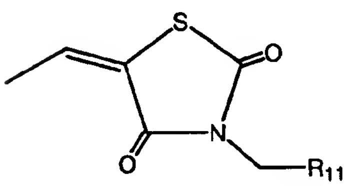
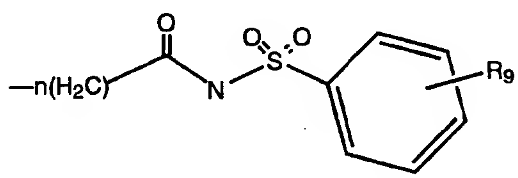
, , ,

, , ,

 ,  ,

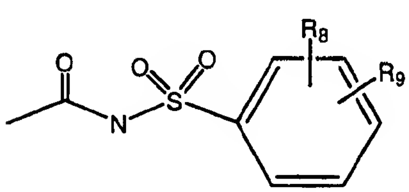
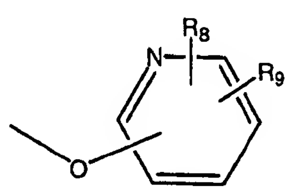
 ,  ,

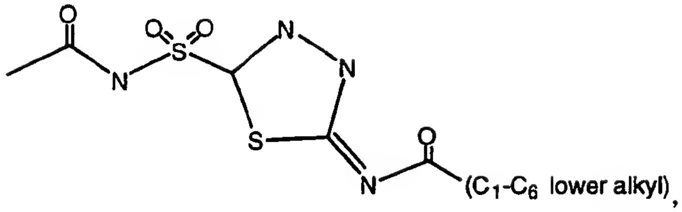
 ,  , or

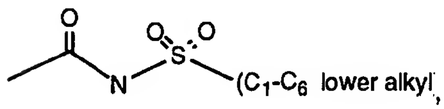
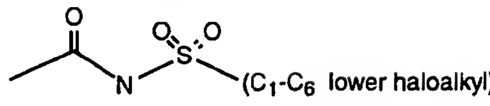
  ;

R_8 and R_9 are independently selected from H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), or -N(C_1-C_6 alkyl)$_2$;

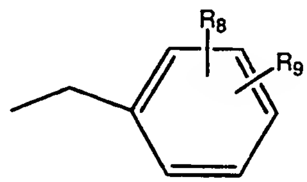
R_{10} is selected from the group of H, halogen, $-CF_3$, -OH, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, $-C_1$-C_6 alkyl, -O-C_1-C_6 alkyl, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,

 ,  , or

,

,  ;

R_{11} is selected from H, C_1-C_6 lower alkyl, $-CF_3$, -COOH, $-(CH_2)_n$-COOH, $-(CH_2)_n$-C(O)-COOH, or

 ;

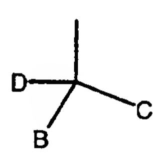
n is an integer from 0 to 3;

R_4 is selected from H, $-CF_3$, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or halogen;

R_5 is selected from C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, $-(CH_2)_n$-C_3-C_5 cycloalkyl or the groups of:

a) -C(O)-O-$(CH_2)_n$-C_3-C_5 cycloalkyl, $-(CH_2)_n$-phenyl, $-(CH_2)_n$-S-phenyl, -$(CH_2)_n$-phenyl-O-phenyl, $-(CH_2)_n$-phenyl-CH_2-phenyl, $-(CH_2)_n$-O-phenyl-CH_2-phenyl, -$(CH_2)_n$-phenyl-(O-CH_2-phenyl$)_2$, -C(O)-O-phenyl, -C(O)-O-benzyl, -C(O)-O-pyridinyl, -C(O)-O-napthyl, $-(CH_2)_n$-S-napthyl, $-(CH_2)_n$-S-pyridinyl, $-(CH_2)_n$-pyridinyl or $-(CH_2)_n$-napthyl, the phenyl, pyridinyl and napthyl rings of these groups being optionally substituted by from 1 to 3 substituents selected from H, halogen, $-CF_3$, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH_2, or $-NO_2$; or

b) a moiety of the formula $-(CH_2)_n$-A, $-(CH_2)_n$-S-A, or $-(CH_2)_n$-O-A, wherein A is the moiety:



wherein

D is H, C_1-C_6 lower alkyl, C_1-C_6 lower alkoxy, or $-CF_3$;

B and C are independently selected from phenyl, pyridinyl, furyl, thienyl or pyrrolyl groups, each optionally substituted by from 1 to 3, substituents selected from H, halogen, -CF_3, -OH, -C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, or $-NO_2$;
or a pharmaceutically acceptable salt thereof.

13. A compound of Claim 1 which is selected from:

a) 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

b) Cyclopentyl-N-{3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl) benzyl]-1-propyl-1H-indol-5-yl}carbamate;

c) 4-[(1-benzhydryl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

d) 4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(2-naphthylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

e) 4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(cyclopropylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

f) 4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(cyclopropylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

g) 4-{[5-{[(cyclopentyloxy)carbonyl]amino}-1-(4-pyridinylmethyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

h) 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-isopropyl-1H-indol-3yl)methyl]-3-methoxybenzoic acid;

i) 4-[(1-cyclopentyl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid; or

j) 4-[(1-benzhydryl-5-{[(butylamino)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

or a pharmaceutically acceptable salt thereof.

14. A compound of Claim 1 which is selected from:

a) 4-({1-benzhydryl-5-[(methylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

b) 4-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

c) 4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

d) 4-[(1-benzhydryl-5-fluoro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

e) 4-[(1-benzhydryl-5-methyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

f) 4-[(5-benzhydryl-5H-[1,3]dioxolo[4,5-f]indol-7-yl)methyl]-3-methoxybenzoic acid;

g) 4-[(1-benzhydryl-5-cyano-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

h) 4-{[1-benzhydryl-5-(methylsulfonyl)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid; or

j) cyclopentyl-N-{1-benzhydryl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl] amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

or a pharmaceutically acceptable salt thereof.

15. A comound of Claim 1 which is selected from:

a) Cyclopentyl-N-{3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino} carbonyl)benzyl]-1-propyl-1H-indol-5-yl}carbamate;

b) N-{1-(cyclopropylmethyl)-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl] amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

c) cyclopentyl-N-[3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino} carbonyl)benzyl]-1-(4-pyridinylmethyl)-1H-indol-5-yl]carbamate;

d) cyclopentyl-N-[3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl) benzyl]-1-(2-naphthylmethyl)-1H-indol-5-yl]carbamate;

e) cyclopentyl-N-{1-isopropyl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl] amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

f) cyclopentyl-N-{1-cyclopentyl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl] amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

g) cyclopentyl N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl) sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

h) cyclopentyl N-[1-benzhydryl-3-(2-methoxy-4-{[(methylsulfonyl)amino] carbonyl}benzyl)-1H-indol-5-yl]carbamate;

i) N-{1-benzhydryl-3-[4-({[(2-chlorophenyl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}; or

j) cyclopentyl N-(3-{4-[({[5-(acetylimino)-4-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1-benzhydryl-1H-indol-5-yl)carbamate;

or a pharmaceutically acceptable salt thereof.

16. A compound of Claim 1 which is selected from:

a) cyclopentyl N-(1-benzhydryl-3-{4-[({[5-(dimethylamino)-1-naphthyl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1H-indol-5-yl)carbamate;

b) cyclopentyl N-[1-benzhydryl-3-(4-{[(benzylsulfonyl)amino]carbonyl}-2-methoxybenzyl)-1H-indol-5-yl]carbamate;

c) cyclopentyl N-{1-benzhydryl-3-[4-({[(2,4-dimethyl-1,3-thiazol-5-yl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}carbamate;

d) cyclopentyl N-{1-benzhydryl-3-[4-({[(3,5-dimethyl-4-isoxazolyl)sulfonyl]amino}carbonyl)-2-methoxybenzyl]-1H-indol-5-yl}carbamate;

e) cyclopentyl N-(3-{4-[({[5-(acetylamino)-1,3,4-thiadiazol-2-yl]sulfonyl}amino)carbonyl]-2-methoxybenzyl}-1-benzhydryl-1H-indol-5-yl)carbamate;

f) cyclopentyl N-(1-benzhydryl-3-{2-methoxy-4-[({[4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)phenyl]sulfonyl}amino)carbonyl]benzyl}-1H-indol-5-yl)carbamate;

g) N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoyl}-2-methylbenzenesulfonamide;

h) N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro)methanesulfonamide;

i) N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]-3-methoxybenzoyl}-2-methylbenzenesulfonamide; or

j) N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro)methanesulfonamide;

or a pharmaceutically acceptable salt thereof.

17. A compound of Claim 1 which is selected from:

a) N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}cyclopentanecarboxamide;

b) N-[4-({1-benzhydryl-5-[(methylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoyl](trifluoro)methanesulfonamide;

c) N-{4-[(1-benzhydryl-5-{[(butylamino)carbonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoyl}(trifluoro) methane sulfonamide;

d) N-{1-benzhydryl-3-[2-methoxy-4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}cyclopentanecarboxamide;

e) 4-({5-[(cyclopentylcarbonyl)amino]-1-[phenyl(2-pyridinyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

f) N-[4-({1-benzhydryl-5-[(benzylsulfonyl)amino]-1H-indol-3-yl}methyl)-3-methoxybenzoyl](trifluoro)methanesulfonamide;

g) N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}-3-thiophenecarboxamide;

h) Benzyl N-{1-benzhydryl-3-[2-methoxy-4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

g) 4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoic acid;

h) 4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoic acid;

i) 4-[(1-benzhydryl-5-{[(cyclopentyloxy)carbonyl]amino}-1H-indol-3-yl)methyl]benzoic acid; or

j) cyclopentyl N-{1-benzhydryl-3-[4-({[(2-methylphenyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

or a pharmaceutically acceptable salt thereof.

18. A compound of Claim 1 which is selected from:

a) cyclopentyl N-{1-benzhydryl-3-[4-({[(trifluoromethyl)sulfonyl]amino}carbonyl)benzyl]-1H-indol-5-yl}carbamate;

b) N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoyl}(trifluoro)methanesulfonamide;

c) N-{4-[(1-benzhydryl-5-nitro-1H-indol-3-yl)methyl]benzoyl}-2-methylbenzenesulfonamide;

d) N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoyl}-2-methylbenzenesulfonamide;

e) N-{4-[(1-benzhydryl-5-bromo-1H-indol-3-yl)methyl]benzoyl}(trifluoro)methanesulfonamide;

f) 3-({2-[1-(4-benzylbenzyl)-1H-indol-3-yl]-2-oxoacetyl}amino)benzoic acid;

g) 3-({2-[1-(4-{[3,5-bis(trifluoromethyl)phenoxy]methyl}benzyl)-1H-indol-3-yl]-2-oxoacetyl}amino)benzoic acid;

h) 3-{[2-(1-benzhydryl-1H-indol-3-yl)-2-oxoacetyl]amino}benzoic acid;

i) 3-[(2-{1-[3-(4-benzylphenoxy)propyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid; or

j) 3-[(2-{1-[3,4-bis(benzyloxy)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

or a pharmaceutically acceptable salt thereof.

19. A compound of Claim 1 which is selected from:

a) 3-[(2-{1-[2-(benzylsulfonyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

b) 3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)amino]benzoic acid;

c) 2-[4-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)piperazino]acetic acid;

d) 2-[1-({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)-3-oxo-2-piperazinyl]acetic acid;

e) 2-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}methyl)amino]-3-hydroxypropanoic acid;

f) 2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetic acid:

g) 2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetic acid;

h) 3-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetyl} amino)benzoic;

i) 5-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]isophthalic acid; or

j) 3-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

or a pharmaceutically acceptable salt thereof.

20. A compound of Claim 1 which is selected from:

a) 5-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-2-oxoacetyl}amino)-2-[(5-chloro-3-pyridinyl)oxy]benzoic acid;

b) 5-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}-2-oxoacetyl)amino]-2-[(5-chloro-3-pyridinyl)oxy]benzoic acid;

c) 2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]-N-[3-({[(4-methylphenyl)sulfonyl]amino}carbonyl)phenyl]-2-oxoacetamide;

d) 2-[5-bromo-1-(cyclopropylmethyl)-1H-indol-3-yl]acetic acid;

e) 2-[1-(cyclopropylmethyl)-5-(2-thienyl)-1H-indol-3-yl]acetic acid;

f) 2-{1-(cyclopropylmethyl)-5-[3-(trifluoromethyl)phenyl]-1H-indol-3-yl}acetic acid;

g) 2-[5-(1-benzofuran-2-yl)-1-benzyl-1H-indol-3-yl]acetic acid;

h) 2-(1-benzyl-5-phenyl-1H-indol-3-yl)acetic acid;

i) 4-{[5-((E)-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}methylidene)-2,4-dioxo-1,3-thiazolan-3-yl]methyl}benzoic acid; or

j) 2-[5-((E)-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}methylidene)-2,4-dioxo-1,3-thiazolan-3-yl]acetic acid;

or a pharmaceutically acceptable salt thereof.

21. A compound of Claim 1 which is selected from:

a) 3-{1-[3-(3-benzylphenoxy)propyl]-1H-indol-3-yl}propanoic acid;

b) 3-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}propanoic acid;

c) N-(1-benzhydryl-3-{3-[(methylsulfonyl)amino]-3-oxopropyl}-1H-indol-5-yl)cyclopentanecarboxamide;

d) (E)-3-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-propenoic acid;

e) N-(1-benzhydryl-3-{(E)-3-[(methylsulfonyl)amino]-3-oxo-1-propenyl}-1H-indol-5-yl)cyclopentanecarboxamide;

f) (E)-3-{1-benzhydryl-5-nitro-1H-indol-3-yl}-2-propenoic acid ester;

g) N-((E)-3-{1-benzhydryl-5-nitro-1H-indol-3-yl}-2-propenoyl)methanesulfonamide;

h) 4-{[1-benzhydryl-5-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

i) 4-{[5-({[2-(acetylamino)-4-methyl-1,3-thiazol-5-yl]sulfonyl}amino)-1-benzhydryl-1H-indol-3-yl]methyl}-3-methoxybenzoic acid; or

j) 4-[(1-benzhydryl-5-{[(4-chloro-3-nitrophenyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

or a pharmaceutically acceptable salt thereof.

22. A compound of Claim 1 which is selected from:

a) 4-[(1-benzhydryl-5-{[(dimethylamino)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

b) 4-{[1-benzhydryl-5-({[4-(trifluoromethoxy)phenyl]sulfonyl}amino)-1H-indol-3-yl]methyl}-3-methoxybenzoic acid;

c) 4-[(1-benzhydryl-5-{[(2-methylphenyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

d) 4-[(1-benzhydryl-5-{[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

e) 4-[(1-benzhydryl-5-{[(3,5-dimethyl-4-isoxazolyl)sulfonyl]amino}-1H-indol-3-yl)methyl]-3-methoxybenzoic acid;

f) cyclopentyl N-{3-[4-(aminocarbonyl)-2-methoxybenzyl]-1-benzhydryl-1H-indol-5-yl}carbamate;

g) cyclopentyl N-{1-benzhydryl-3-[2-methoxy-4-(1H-1,2,3,4-tetraazol-5-yl)benzyl]-1H-indol-5-yl}carbamate;

h) 4-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]-3-thiophenecarboxylic acid;

i) 3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]benzoic acid; or

j) 3-[({1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}carbonyl)amino]propanoic acid;

or a pharmaceutically acceptable salt thereof.

23. A compound of Claim 1 which is selected from:

a) N-[1-benzhydryl-3-({[(2-methylphenyl)sulfonyl]amino}carbonyl)-1H-indol-5-yl]cyclopentanecarboxamide;

b) 3-[(2-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-oxoacetyl)amino]propanoic acid;

c) 3-[(2-{1-benzhydryl-5-[(cyclopentylcarbonyl)amino]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

d) 3-({2-[1-(4-benzylbenzyl)-5-(benzyloxy)-1H-indol-3-yl]acetyl}amino)benzoic acid;

e) 3-[(2-{5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-1H-indol-3-yl}acetyl)amino] benzoic acid;

f) 5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-2-methyl-1H-indole-3-carboxylic acid;

g) 5-[({5-(benzyloxy)-1-[2,4-bis(trifluoromethyl)benzyl]-2-methyl-1H-indol-3-yl}carbonyl)amino]isophthalic acid;

h) 5-(benzyloxy)-2-methyl-1-(2-naphthylmethyl)-1H-indole-3-carboxylic acid;

i) 5-({[5-(benzyloxy)-2-methyl-1-(2-naphthylmethyl)-1H-indol-3-yl]carbonyl} amino)isophthalic acid; or

j) 1-benzyl-5-(benzyloxy)-2-methyl-1H-indole-3-carboxylic acid;
or a pharmaceutically acceptable salt thereof.

24. A compound of Claim 1 which is selected from:

a) 3-[(2-{5-(benzyloxy)-1-(4-chlorobenzyl)-2-[(2-naphthylsulfanyl)methyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

b) 3-[(2-{5-(benzyloxy)-1-methyl-2-[(2-naphthylsulfanyl)methyl]-1H-indol-3-yl}-2-oxoacetyl)amino]benzoic acid;

c) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-2,6-dimethylphenoxy} acetic acid;

d) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxyphenoxy} acetic acid;

e) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]phenoxy}acetic acid;

f) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-chlorophenoxy}acetic acid;

g) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-2-methoxyphenoxy}acetic acid;

h) (E)-4-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]phenoxy}-2-butenoic acid;

i) 4-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-4-oxobutanooic acid; or

j) Sodium 3-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-3-oxopropanoic acid;
or a pharmaceutically acceptable salt thereof.

25. A compound of Claim 1 which is selected from:

a) 2-{4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]anilino}-2-oxoacetic acid;

b) 2-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]cyclopropanecarboxylic acid;

c) 2-[(1-benzhydryl-6-chloro-5-fluoro-1H-indol-3-yl)methyl]cyclopropane carboxylic acid;

d) 2-[(1-benzhydryl-5,6-dichloro-1H-indol-3-yl)methyl]cyclopropanecarboxylic acid;

e) 2-({1-[bis(4-hydroxyphenyl)methyl]-6-chloro-1H-indol-3-yl}methyl) cyclopropanecarboxylic acid;

f) '4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-hydroxybenzoic acid;

g) '4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-(3-hydroxypropoxy) benzoic acid;

h) '4-({1-[(4-aminophenyl)(phenyl)methyl]-6-chloro-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

i) '4-({6-chloro-1-[(4-methoxyphenyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

j) '4-({1-[bis(4-methoxyphenyl)methyl]-6-chloro-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

k) '4-({6-chloro-1-[(2-morpholinophenyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

l) 4-({6-chloro-1-[(2,4-dimethoxy-5-pyrimidinyl)(phenyl)methyl]-1H-indol-3-yl}methyl)-3-methoxybenzoic acid;

m) '4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxybenzoic acid; or

n) 2-({4-[(1-benzhydryl-6-chloro-1H-indol-3-yl)methyl]-3-methoxybenzoyl} amino)acetic acid;

or a pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

27. A pharmaceutical composition comprising a compound of Claim 5, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

28. A pharmaceutical composition comprising a compound of Claim 7, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

29. A pharmaceutical composition comprising a compound of Claim 8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

30. A pharmaceutical composition comprising a compound of Claim 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

31. A pharmaceutical composition comprising a compound of Claim 10, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

32. A pharmaceutical composition comprising a compound of Claim 11, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

33. A method for treating inflammation in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof.